	FI 8603186	A	19870405	FI 86-3186	19860805
	FI 92878	B	19940930		
	FI 92878	C	19950110		
	JP 07311200	A2	19951128	JP 95-10194	19950125
	JP 2575338	B2	19970122		
PRAI	US 85-784857	19851004			
	EP 86-300336	19860117			

AB A method is described for measuring the concn. of a free ligand in biol. fluids in the presence of bound ligand and endogenous binding proteins, without disturbing the equil. between the free and the protein-bound ligand. The method comprises (1) incubating a sample with (i) a labeled ligand analog which does not bind to some of the endogenous binding proteins but does bind to .ltoreq.1 other endogenous binding protein, (ii) a specific ligand binder, and (iii) .gtoreq.1 specific inhibitor that inhibits the binding of the ligand analog to its endogenous binding protein; (2) sepg. the bound from the unbound ligand analog; and (3) detg. the concn. of the free ligand in the sample by comparing the bound fraction of the ligand analog to a calibration curve obtained using free ligand calibrators. Conditions for the detn. of T4 were worked out and comprise (1) using 125I-labeled N-L-thyroxinesuccinimide as the ligand analog (which binds to albumin, the endogenous binding protein, in the absence of inhibitors); (2) employing a 1:250,000 diln. of antibodies to T4 as the specific ligand, which has a lower affinity than albumin for the ligand analog; and (3) using 5 mg Na salicylate/mL as the inhibitor, which abolishes binding of the ligand analog to albumin and allows 49.2% binding of ligand analog to the antibodies.

=> fil hom

FILE 'HOME' ENTERED AT 11:24:12 ON 23 DEC 1998

Esophagitis; [3226]_Acute Therapy; [3226]_Maintenance Therapy; [3224,_214] Other Uses; [3604]_Nervous System Effects; [3604]_GI Effects; [3604]_Dermatologic and Sensitivity Reactions; [3604]_Hematologic Effects; [3604]_Renal and Genitourinary Effects; [3604]_Hepatic Effects; [3604]_Ocular Effects; [3604]_Endocrine Effects; [3604]_Cardiovascular Effects; [3604]_Other Adverse Effects; [3644]_Precautions and Contraindications; [3644]_Pediatric Precautions; [3664]_Mutagenicity and Carcinogenicity; [3654]_Pregnancy, Fertility, and Lactation; [3774]_Food and Antacids; [3774]_Clarithromycin; [3774]_Propantheline Bromide; [3704]_Smoking; [3774]_Effects on Hepatic Clearance of Drugs; [3776]_Coumarin Anticoagulants; [3776]_Theophyllines; [3776]_Benzodiazepines; [3776]_beta-Adrenergic Blocking Agents; [3776]_Acetaminophen; [3776]_Phenytoin; [3774]_Other Drugs; [3574]_Administration; [3576]_Oral Administration; [3576]_IM Injection; [3576]_Intermittent Direct IV Injection; [3576]_Intermittent IV Infusion; [3576]_Continuous IV Infusion; [3524]_Dosage; [3526]_Parenteral Dosage; [3526]_Oral Dosage; [3526]_Duodenal Ulcer.; [3526]_Pathologic GI Hypersecretory Conditions.; [3526]_Gastric Ulcer.; [3526]_Gastroesophageal Reflux.; [3526]_Erosive Esophagitis.; [3526]_Self-medication.; [3564]_Dosage in Renal Impairment; [3404]_Ranitidine Bismuth Citrate; [3404]_Ranitidine Hydrochloride; [3424]_Ranitidine Hydrochloride in Sodium Chloride
? ds

Another

Set	Items	Description
S9	86	AU=(EL SHAMI, A? OR EL SHAMI A? OR ELSHAMI, A? OR ELSHAMI - A? OR SHAMI A? OR SHAMI, A?)
S10	86	S9 NOT S7
S11	0	S10 AND S1

? log y

23dec98 12:04:03 User219783 Session D1433.4

Devi, S.
09/036819


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=> fil reg; d que l3; d que l8

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DICTIONARY FILE UPDATES: 22 DEC  98  HIGHEST RN 215853-88-6

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L1            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  THYROXINE/CN
L2            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRIIODOTHYRONINE/CN
L3            2 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 OR L2


L4            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "2,4-DINITROPHENOL"/CN

L5            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ("SODIUM SALICYLATE"/CN
                 OR "SODIUM SALICYLATE (NAO3C7H5)"/CN)
L6            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  SULFOBROMOPHTHALEIN/CN

L7            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "OLEIC ACID"/CN
L8            4 SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 OR L5 OR L6 OR L7

=> fil caplu

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FILE LAST UPDATED: 23 Dec 1998  (981223/ED)

  This file contains CAS Registry Numbers for easy and accurate
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=> d que

L1             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  THYROXINE/CN
L2             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  TRIIODOTHYRONINE/CN
L3             2 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 OR L2
L4             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "2,4-DINITROPHENOL"/CN

L5             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ("SODIUM SALICYLATE"/CN
                   OR "SODIUM SALICYLATE (NAO3C7H5)"/CN)
L6             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  SULFOBROMOPHTHALEIN/CN

L7             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "OLEIC ACID"/CN
L8             4 SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 OR L5 OR L6 OR L7
L9         27613 SEA FILE=CAPLUS ABB=ON  PLU=ON  L3 OR THYROXINE OR
                   TRIIODOTHYRONINE OR TRI(W)(IODOTHYRONINE OR IODO
                   THYRONINE) OR TRIIODO THYRONINE
L10          266 SEA FILE=CAPLUS ABB=ON  PLU=ON  L9 AND (L8 OR 2(W)4(W)(DI
                   NITROPHENOL OR DI(W)(NITROPHENOL OR NITRO PHENOL) OR
                   DINITRO PHENOL) OR (NA OR SODIUM)(W)SALICYLATE OR
                   SULFOBROMOPHTHALEIN OR SULPHOBROMOPHTHALEIN OR (SULPHO
                   OR SULFO)(W)(BROMOPHTHALEIN OR BROMO PHTHALEIN) OR
                   OLEIC)
L11           20 SEA FILE=CAPLUS ABB=ON  PLU=ON  L10 AND LIGAND

=> d 1-20 .bevstr


L11  ANSWER 1 OF 20  CAPLUS  COPYRIGHT 1998 ACS
AN   1994:450249  CAPLUS
DN   121:50249
TI   Computer-assisted molecular modeling of benzodiazepine and
     thyromimetic inhibitors of the HepG2 iodothyronine membrane
     transporter
AU   Kragie, Laura; Forrester, Maureen L.; Cody, Vivian; McCourt, Mary
CS   Fac. Nat. Sci. Math., State Univ. New York, Buffalo, Amherst, NY,
     14260, USA
SO   Mol. Endocrinol. (1994), 8(3), 382-91
     CODEN: MOENEN; ISSN: 0888-8809
DT   Journal
LA   English
AB   T3 cellular uptake is inhibited in the presence of benzodiazepines
     (BZs). The structure-activity relationship of BZ inhibition
     correlates strongly with halogen substitution of the nonfused Ph
     ring and indicates that this ring is required for activity. A
     structure-activity series of thyromimetic (TH) inhibitors of the
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HepG2 iodothyronine transporter further point out the crit. importance of the amino group of the alanine side chain, its L-stereo configuration, and the size of the substituents of the inner and outer Ph rings. A third series of compds., reported to interact at related sites, were inactive as HepG2 iodothyronine transport inhibitors, and therefore the potent inhibitors were restricted to the BZ and TH compds. Using both of these BZ and TH structure-activity series along with computer-assisted mol. modeling techniques, the authors detd. which chem. structural components were important at the transporter interaction site. By superimposing structures from active chems., excluding residues from poor inhibitors, and incorporating mol. electropotential data, the authors developed a five-point model of BZ conformational similarity to the endogenous transporter **ligand**, L-T3: the alkyl substitution at the N1 of the BZ ring seems to stimulate the alanine side chain of T3, and the electroneg. halogen and oxygen atoms of substituents at R3/R7/R2'/R4' of BZ form a pyrimidyl pharmacophore that seems to correspond with the 3-1/5-1/3'-1/4'-OH substituents of T3, resp. These points, suggesting a tilted cross-bow formation, may be sites for **ligand** interaction with the iodothyronine transporter.

IT **6893-02-3**, **Triiodothyronine**
RL: BIOL (Biological study)
(binding of, by membrane iodothyronine transporter, benzodiazepine and thyromimetic inhibitors of, structure in relation to)

IT **51-48-9**, **Thyroxine**, biological studies
71-67-0, Bromosulfophthalein
RL: BIOL (Biological study)
(**triiodothyronine** binding by iodothyronine transporter inhibition by, structure in relation to)

L11 ANSWER 2 OF 20 CAPLUS COPYRIGHT 1998 ACS
AN 1994:293590 CAPLUS
DN 120:293590
TI Separation method with auxiliary **ligand**-binder pairs in immunological detection of multiple analytes
IN Abuknesha, Ramadan Arbi
PA GEC-Marconi Ltd., UK
SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9403807	A1	19940217	WO 93-GB1627	19930802

W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT,

	SE				
	GB 2270976	A1	19940330	GB 92-19743	19920918
	GB 2261948	A1	19930602	GB 92-24897	19921127
	GB 2261949	A1	19930602	GB 92-24898	19921127
	EP 653065	A1	19950517	EP 93-917967	19930802
	R: DE, FR				

PRAI GB 92-16450 19920803
GB 92-16683 19920806
GB 92-19743 19920918
GB 92-20722 19921001
GB 92-24897 19921127
GB 92-24898 19921127
GB 91-25204 19911127
GB 91-25218 19911127
WO 93-GB1627 19930802

AB A sepn. method which finds application in immunol. detection, a method suitable for use in detection, a sensor, and a test kit are disclosed. The invention provides a sepn. method suitable for use in an immunol. method for the detection of >1 species, which includes the use of >1 auxiliary **ligand**-binder pairs, the auxiliary **ligand** of each of the plurality of auxiliary **ligand**-binder pairs being provided on a support material. The invention also provides a sepn. method which includes the use of a plurality of auxiliary **ligand**-binder pairs, an auxiliary **ligand** of one auxiliary **ligand**-binder pair being provided on a support material and a binder of another auxiliary **ligand**-binder pair, which pair comprises an auxiliary **ligand**-auxiliary binder pair, being provided on a support material. The invention is useful for detection of multiple analytes. 17.beta.-Estradiol, progesterone and L-**thyroxine** were selected as analytes to illustrate the use of >1 auxiliary **ligand**-auxiliary binder pairs in sepns. of multiple analytes for immunol. detection. The auxiliary **ligands** used were 7-hydroxy-4-methylcoumarin-3propionic acid, 2-(4-aminophenyl)-6-methylthiazole hemiglutarate, and 2-phenyl-4-quinoline carboxylic acid; auxiliary binders were antibodies to these **ligands**.

IT **51-28-5**, **2,4-Dinitrophenol**,
analysis
RL: ANST (Analytical study)
(as auxiliary **ligand**, antibody as auxiliary binder to, in sepn. in multiple analyte immunol. detection)

IT **51-48-9**, L-**Thyroxine**, analysis
RL: ANT (Analyte); ANST (Analytical study)
(detection of, immunochem., auxiliary **ligand**-binder pairs in sepn. in relation to)

L11 ANSWER 3 OF 20 CAPLUS COPYRIGHT 1998 ACS
AN 1994:239683 CAPLUS
DN 120:239683

TI Preparation of controlled-size inorganic particles for use in separations, assays, as magnetic molecular switches, and as inorganic liposomes for medical applications

IN Chagnon, Mark S.; Carter, Michelle J.; Ferris, John R.; Gray, Maria A.; Hamilton, Tracy J.; Rudd, Edwin A.

PA Molecular Bioquest, Inc., USA

SO PCT Int. Appl., 101 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9326019	A1	19931223	WO 93-US5595	19930608
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5389377	A	19950214	US 92-958646	19921007
	US 5441746	A	19950815	US 93-57687	19930505
	EP 645048	A1	19950329	EP 93-915304	19930608
	R: DE, FR, GB, SE				
	JP 08500700	T2	19960123	JP 93-501742	19930608

PRAI US 92-894260 19920608
US 92-911962 19920710
US 92-958646 19921007
US 93-57687 19930505
US 89-455071 19891222
US 90-566169 19900810
WO 93-US5595 19930608

AB Inorg. oxides of substantially uniform particle size distribution are prepd. by contacting aq. solns. of an inorg. salt and an inorg. base across a porous membrane, wherein the membrane contains pores which allow for pptn. of a substantially monodispersed size of inorg. oxide particles on one side of the membrane and pptn. of a salt of the corresponding base on a second side of the membrane. The prepd. particles can be coated with an organo-metallic polymer having attached thereto an org. functionality to which a variety of org. and/or biol. mols. can be coupled. The coupled particles may be used for in vitro or in vivo systems involving sepns. steps or the directed movement of coupled mols. to particular sites, including immunol. assays, other biol. assays, biochem. or enzymic reactions, affinity chromatog. purifn., cell sorting, and diagnostic and therapeutic uses. In a further embodiment, described herein are liposome compns. which comprise the substantially uniform size inorg. core coated with an amphipathic org. compd. and further coated with a second amphipathic vesicle-forming lipid. Also disclosed are novel Ph lipid compds. which serve as the vesicle-forming lipid. When the magnetic particles are electromagnetic wave-absorbing surface-modified particles, such

particles provide for the prepn. of liposome compns. which offer a method for the treatment of cancer, as well as infectious diseases. Electromagnetic wave-absorbing ferrites were prepd. by the hydroxide gel process from FeCl3, CaCl2, and ZnCl2 or from FeCl3, FeCl2, and MnCl2 using NaOH and O2. The ferrite particles were coated with **oleic** acid and then treated with a second layer of Ph lipid prepd. from 5-aminoisophthalic acid and methoxypolyoxyethylene imidazoly carbonyl. The lipid-coated ferrites and uncoated ferrites (controls) were incubated with MDCK cells grown above a colony of rat neuroblastoma cells and then exposed to a frequency of 20,000 mHz for 3 min. None of the bare ferrite particles were permeable to the MDCK membrane and so had no effect on the cancer cells; the lipid-coated ferrites were permeable, heated up upon exposure to the electromagnetic wave, and killed all the cancer cells. Lipid-coated ferrites (contg. all Fe) that did not absorb electromagnetic waves were able to cross the cell barrier but were unable to kill the neuroblastoma cells.

IT **51-48-9**, **Thyroxine**, analysis **6893-02-3**, **Triiodothyronine**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, by immunoassay using inorg. oxide particles coated with organometallic polymer functionalized to bind antibodies)

IT **112-80-1**, **Oleic** acid, uses
RL: USES (Uses)
(uniform-sized inorg. core particles coated with, amphipathic vesicle-forming lipid as second coating on, for liposomes)

L11 ANSWER 4 OF 20 CAPLUS COPYRIGHT 1998 ACS
AN 1994:239672 CAPLUS
DN 120:239672
TI Immunological detection using two detectable labels
IN Abuknesha, Ramadan Arbi
PA GEC-Marconi Ltd., UK
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9403811	A1	19940217	WO 93-GB1628	19930802
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
GB 2270976	A1	19940330	GB 92-19743	19920918
GB 2260609	A1	19930421	GB 92-21578	19921014
GB 2260609	B2	19960522		
GB 2261948	A1	19930602	GB 92-24897	19921127
GB 2261949	A1	19930602	GB 92-24898	19921127

	EP 660935	A1	19950705	EP 93-917968	19930802
	R: DE, FR				
	US 5723304	A	19980303	US 95-381826	19950227
PRAI	GB 92-16465	19920803			
	GB 92-19743	19920918			
	GB 92-20722	19921001			
	GB 92-21578	19921014			
	GB 92-24897	19921127			
	GB 92-24898	19921127			
	GB 91-22180	19911018			
	GB 91-25204	19911127			
	GB 91-25218	19911127			
	WO 93-GB1628	19930802			

AB A method of detection, sensor, and test kit for immunoassays are described which involve ratiometric detection of 2 detectable species which are detectable independently of one another and are influenced independently by the analyte. use an auxiliary **ligand** (e.g. an auxiliary antigen) and a binder (e.g. antibody) for the auxiliary **ligand** for ratiometric detection of 2 detectable species. This improves the accuracy and precision of measurement of a signal by avoiding abs. measurements, e.g. where one of the detectable species is influenced by the presence of the analyte while the other is not, and the 2 detectable species can be detected independently. Thus, in an immunoassay for L-**thyroxine**, an antibody to **thyroxine** was conjugated with 5(6)-carboxyfluorescein N-hydroxysuccinimide ester. A 2nd antibody directed to 2-phenyl-4-quinolinecarboxylic acid was conjugated with **thyroxine**-N-amidoglutaric acid N-hydroxysuccinimide ester and with 7-amino-4-methylcoumarin-3-propionic acid N-hydroxysuccinimide ester. Polystyrene assay tubes coated with a 2-phenyl-4-quinolinecarboxylic acid-ovalbumin conjugate received std. solns. or samples contg. **thyroxine** and fluorescein-labeled primary antibody and then the 2nd antibody conjugate. After incubation and washing, the fluorescence bound to the tubes was measured at 510 nm (fluorescein) and 450 nm (7-amino-4-methylcoumarin). The fluorescence intensity for fluorescein increased with increasing **thyroxine** concn., whereas that for the coumarin remained relatively const. The ratios of the 2 fluorescence intensities was plotted as a function of **thyroxine** concn. for use as a calibration curve.

IT **51-28-5**, **2,4-Dinitrophenol**,
uses
RL: USES (Uses)
(as auxiliary **ligand**, in immunoassay with multiple label detection)

IT **51-48-9**, L-**Thyroxine**, analysis
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, by immunoassay with multiple label detection)

L11 ANSWER 5 OF 20 CAPLUS COPYRIGHT 1998 ACS
AN 1994:51745 CAPLUS
DN 120:51745
TI A naturally occurring furan fatty acid enhances drug inhibition of **thyroxine** binding in serum
AU Lim, Chen Fee; Stockigt, Jan R.; Curtis, Andrea J.; Wynne, Kenneth N.; Barlow, John W.; Topliss, Duncan J.
CS Ewen Downie Metab. Unit., Alfred Hosp., Melbourne, 3181, Australia
SO Metab., Clin. Exp. (1993), 42(11), 1468-74
CODEN: METAAJ; ISSN: 0026-0495
DT Journal
LA English
AB The authors studied the **thyroxine** (T4)-displacing effects of a naturally occurring, highly albumin-bound furanoid acid that accumulates in serum in renal failure to concns. in excess of 0.2 mmol/L. This substance, 3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid (CMPF), has been shown to displace acidic drugs from albumin binding. The effects of CMPF on **ligand** binding were assessed in the following systems: (1) T4 binding to T4-binding globulin (TBG) and transthyretin (TTR), (2) T4 binding in undiluted serum, (3) T4-displacing potency of fenclofenac, furosemide, diflunisal, and aspirin in undiluted sperm, (4) serum binding of [14C]-drug prepns., and (5) serum binding of [14C]-**oleic** acid. CMPF had a minor direct effect on T4 binding to TBG comparable in relative affinity to that of aspirin, i.e., almost 7 orders of magnitude less than T4 itself. CMPF alone at a concn. of 0.3 mmol/L, which produced only a 10% to 14% increase in free T4 augmented the T4-displacing effects of high therapeutic concns. of the various drugs in undiluted serum as follows: furosemide by 180%, fenclofenac by 160%, diflunisal by 130%, and aspirin by 40%. In the presence of fenclofenac, increments of CMPF from 0.075 to 0.3 mmol/L progressively augmented the T4-displacing effect of this drug, assocd. with a progressive increase in its calcd. free concn. CMPF also inhibited the binding of [14C]-**oleic** acid, suggesting that in some situations CMPF could also indirectly influence thyroid hormone binding by increasing the unbound concn. of nonesterified fatty acids (NEFA), as previously described. CMPF at a concn. of 1 mmol/L did not inhibit charcoal or talc uptake of **triiodothyronine** (T3) or T4. These findings indicate that CMPF can inhibit specific T4 binding in serum by increasing the free concn. of direct competitors. Such "cascade effects" on thyroid hormone binding could influence both the circulating concns. and tissue delivery of thyroid hormones in renal failure and crit. illness.
IT **112-80-1**, **Oleic** acid, biological studies
RL: BIOL (Biological study)
(blood serum binding of, CMPF effect on, renal failure in relation to)
IT **51-48-9**, **Thyroxine**, biological studies

RL: BIOL (Biological study)
(blood serum binding of, CMPF inhibition of, direct drug competitor displacement in, renal failure in relation to)
IT **6893-02-3, Triiodothyronine**
RL: BIOL (Biological study)
(uptake of, by charcoal or talc, CMPF effect on)

L11 ANSWER 6 OF 20 CAPLUS COPYRIGHT 1998 ACS
AN 1994:4026 CAPLUS
DN 120:4026
TI Method for the quantitative determination of a free form of substances present in biological fluids
IN Romelli, Pier Bruno; Chiodoni, Giovanni; Ringhini, Roberto
PA Technogenetics S.r.l., Italy
SO Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 565949	A2	19931020	EP 93-105327	19930331
	EP 565949	A3	19940105		
	R: BE, DE, ES, FR, GB, IT				
	US 5382530	A	19950117	US 92-997735	19921230
PRAI	IT 92-MI910		19920414		

AB Disclosed is a method for detg. the free fraction of analytes present in biol. fluids in a free form which is in equil. with a form bound to .gtoreq.1 endogenous **ligand**. This method comprises: a) contacting the fluid with a 1st exogenous **ligand** L1 capable of sequestering an analyte A in a quantity proportionate to the free fraction; b) in the presence of a predetd. quantity of a 2nd exogenous **ligand** L2 (which binds to A as well as to labeled analyte M), contacting the formed L1-A complex with M and with a dissocg. agent able to dissoc. the sequestered A; and c) detg. the concn. of A either by measuring the quantity of M bound to L2 or by measuring the quantity of unbound M. Free T4 was detd. in human blood serum by RIA using polystyrene test tubes contg. bound **thyroxine**-binding globulin (as L1) and bound antithyroxine antibody (as L2), 125I-T4 (as labeled analyte), and 8-anilino-1-naphthalenesulfonic acid (as dissocg. agent).
IT **54-21-7, Sodium salicylate**
RL: ANST (Analytical study)
(as dissocg. agent, in assay for free analyte in biol. fluid contg. bound analyte, sequestering **ligand** and second **ligand** and labeled analyte and)
IT **51-48-9, Thyroxine**, analysis
RL: ANST (Analytical study)
(detn. of free, in biol. fluid contg. bound **thyroxine**

using sequestering **ligand** and second **ligand** and dissocg. agent and labeled **thyroxine**)

IT **6893-02-3**, **Triiodothyronine**
RL: ANST (Analytical study)
(detn. of free, in biol. fluid contg. bound **triiodothyronine** using sequestering **ligand** and second **ligand** and dissocg. agent and labeled **triiodothyronine**)

L11 ANSWER 7 OF 20 CAPLUS COPYRIGHT 1998 ACS
AN 1992:400277 CAPLUS
DN 117:277
TI Mechanism of allergic cross-reactions. I. Multispecific binding of ligands to a mouse monoclonal anti-DNP IgE antibody
AU Varga, Janos M.; Kalchschmid, Gertrud; Klein, Georg F.; Fritsch, Peter
CS Dep. Dermatol., Univ. Innsbruck, Innsbruck, 6020, Austria
SO Mol. Immunol. (1991), 28(6), 641-54
CODEN: MOIMD5; ISSN: 0161-5890
DT Journal
LA English
AB A recently developed solid-phase binding assay was used to investigate the specificity of ligand binding to a mouse monoclonal anti-dinitrophenyl IgE (I). All DNP-amino acids, that were tested inhibited the binding of the radio-labeled I to DNP covalently attached to polystyrene microplates; however, the concn. for 50% inhibition varied within four orders of magnitude, DNP-L-serine being the most and DNP-L-proline the least potent inhibitor. In addn. to DNP analogs, a large no. of drugs and other compds. were tested for their ability to compete with DNP for the binding site of I. At the concn. used for screening, 59% of compds. had no significant inhibition; 19% inhibited the binding of I more than 50%. Several families of compds. (tetracyclines, polymyxins, phenothiazines, salicylates, and quinones) that were effective competitors were found. Within these families, changes in the functional groups attached to the family stem had major effects on the affinity of ligand binding. The occurrence frequencies of interactions of ligands with I is in good agreement with the semi-empirical model for multispecific antibody-ligand interations.

L11 ANSWER 8 OF 20 CAPLUS COPYRIGHT 1998 ACS
AN 1992:52007 CAPLUS
DN 116:52007
TI Interactions between **oleic** acid and drug competitors influence specific binding of **thyroxine** in serum
AU Lim, Chen Fee; Curtis, Andrea J.; Barlow, John W.; Topliss, Duncan J.; Stockigt, Jan R.
CS Dep. Med., Monash Univ., Melbourne, 3181, Australia
SO J. Clin. Endocrinol. Metab. (1991), 73(5), 1106-10

CODEN: JCEMAZ; ISSN: 0021-972X
DT Journal
LA English
AB Long-chain nonesterified fatty acids and various drugs may share albumin-binding sites in common. It was questioned whether serum binding of T4 could be indirectly influenced by displacement of drug competitors from these sites by nonesterified fatty acids. The influence of **oleic** acid on drug-induced inhibition of [125I]T4 binding was measured by equil. dialysis, using undiluted serum to avoid diln.-related artifacts. **Oleic** acid (1 mM) alone did not inhibit serum protein binding of T4, but this concn. augmented the inhibitory effects on T4 binding of diflunisal, mefenamic acid, meclofenamic acid, and aspirin. This effect increased with increasing concns. of mefenamic acid, meclofenamic acid, and furosemide. The T4-displacing effect of fenclofenac was not augmented by **oleic** acid. The mechanism of these interactions was studied by examg. (1) **oleic** acid effect on drug binding, and (2) drug effects on **oleic** acid binding in undiluted serum. Increments in added **oleic** acid (0.5-2.0 mM) progressively increased the mean unbound fractions of [14C]aspirin, [14C]diflunisal, and [14C]furosemide, but did not displace [14C]fenclofenac. At the relevant total and free drug concns., the inhibitory effect of **oleic** acid on drug binding and its influence on drug-induced displacement of T4 were concordant in the order: meclofenamic acid > aspirin > mefenamic acid > diflunisal > furosemide > fenclofenac. In contrast, drug-induced increases in the unbound fraction of [14C]**oleic** acid did not correlate with augmentation of T4 displacement. It is concluded that synergistic effects of **oleic** acids and drugs on T4 binding result from drug displacement by **oleic** acid, rather than the reverse effect. Hence, substances that increase the unbound concn. of a competitor by displacing it from albumin can increase its T4-displacing potency. Interactions between various **ligands** may exert a greater hormone-displacing effect than the sum of each alone.

IT **51-48-9**, **Thyroxine**, biological studies
RL: BIOL (Biological study)
(blood serum binding of, drugs and oleate interactions in modulation of)

IT **112-80-1**, **Oleic** acid, biological studies
RL: BIOL (Biological study)
(**thyroxine** binding in blood serum modulation by, drug interactions with)

L11 ANSWER 9 OF 20 CAPLUS COPYRIGHT 1998 ACS
AN 1991:671154 CAPLUS
DN 115:271154
TI Competitive inhibition of T3 binding to .alpha.1 and .beta.1 thyroid hormone receptors by fatty acids

AU Van der Klis, Fiona R. M.; Schmidt, E. D. L.; Van Beeren, H. C.; Wiersinga, W. M.
CS Div. Endocrinol., Acad. Med. Cent., Amsterdam, Neth.
SO Biochem. Biophys. Res. Commun. (1991), 179(2), 1011-16
CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English
AB It was investigated whether fatty acids inhibit the binding of T3 to the .alpha.1 and .beta.1 form of the thyroid hormone receptor. Fatty acids inhibited the binding to T3 to both receptor proteins isolated from a bacterial expression system. The effectiveness of inhibition depended on the chain length and degree of satn. of the fatty acids. The inhibition ot T3 binding to the .alpha.1 and .beta.1 receptor by **oleic** acid was competitive in nature; the Ki value was 5.4 .times. 10-6M for the c-erbA .alpha.1 protein and 3.3 .times. 10-6M for the c-erbA .beta.1 protein. The findings indicated a direct interaction of fatty acids with T3 receptor proteins.
IT **6893-02-3, Triiodothyronine**
RL: BIOL (Biological study)
(thyroid hormone receptor types affinity for, fatty acids effect on)

L11 ANSWER 10 OF 20 CAPLUS COPYRIGHT 1998 ACS
AN 1989:450386 CAPLUS
DN 111:50386
TI Drug competition for **thyroxine** binding to transthyretin (prealbumin): comparison with effects on **thyroxine** -binding globulin
AU Munro, S. L.; Lim, C. F.; Hall, J. G.; Barlow, J. W.; Craik, D. J.; Topliss, D. J.; Stockigt, J. R.
CS Ewen Downie Metab. Unit, Alfred Hosp., Melbourne, 3181, Australia
SO J. Clin. Endocrinol. Metab. (1989), 68(6), 1141-7
CODEN: JCEMAZ; ISSN: 0021-972X
DT Journal
LA English
AB The effect of 26 drugs on T4 binding to transthyretin (TTR; prealbumin) and T4-binding globulin (TBG) was examd. by detg. their ability to inhibit [125I]-labeled T4 binding to TTR isolated from normal human plasma and to serum dild. 1:10,000, resp. The hierarchies for drug inhibition of T4 binding differed greatly for these 2 proteins. Relative to T4, the drugs were much more potent inhibitors of [125I]-labeled T4 binding to TTR than to TBG. Compds. of the anthranilic acid class, such as flufenamic, meclofenamic, and mefenamic acids, interacted particularly strongly with TTR. Flufenamic acid was more potent than T4 itself in inhibiting [125I]-labeled T4 binding [175%; cf. T4), while mefenamic acid, diflunisal, and meclofenamic acid were 20-26% as potent as T4 in their interaction with TTR. The reactivity of diclofenac,

fenclofenac, indomethacin, sulindac, and the diuretic ethacrynic acid was 0.8-2.1% relative to that of T4. In contrast, furosemide, the drug most highly reactive with TBF, was only 0.11% as potent as T4, followed by meclofenamic acid > mefenamic acid > fenclofenac > flufenamic acid > diflunisal > milrinone. Aspirin and **Na salicylate** were, resp., 0.05% and 0.20% as active as unlabeled T4 as inhibitors of [125I]-labeled T4 binding to TTR, but these compds. had only 3-4 .times. 10-6% of the activity of T4 for TBG binding. Diphenylhydantoin had no detectable effect on T4 binding to TTR and was 2.9 .times. 10-4% as reactive as T4 with TBG. Amiodarone did not interact with either binding site. Drug interactions with TTR may be important when this protein becomes a major circulating T4-binding protein, as in patients with complete or partial TBG deficiency, or when serum T4 is markedly elevated. Such interactions may also be important where TTR is the dominant tissue T4-binding protein, as in the choroid plexus. In addn., the drug competitors described here may be useful as probes to further define the structural basis for specific **ligand** interactions with different classes of T4-binding sites.

IT **51-48-9, Thyroxine**, biological studies
RL: BIOL (Biological study)
(binding of, to globulins and prealbumins, drugs effect on)

L11 ANSWER 11 OF 20 CAPLUS COPYRIGHT 1998 ACS
AN 1989:186431 CAPLUS
DN 110:186431
TI Binding activities of **thyroxine** binding globulin versus **thyroxine** binding prealbumin in rat sera: differential modulation by thyroid hormone **ligands**, **oleic** acid and pharmacological drugs
AU Savu, Lia; Vranckx, Roger; Maya, Michelle; Nunez, Emmanuel A.
CS Fac. Med. Xavier Bichat, Paris, 75018, Fr.
SO Biochem. Biophys. Res. Commun. (1989), 159(3), 919-26
CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English
AB Gel equilibration and electrophoresis are used to compare the binding properties of **thyroxine**-binding globulin (TBG) and **thyroxine**-binding prealbumin (TBPA) in rat sera. TBG has the lowest capacity, highest affinity sites for **thyroxine** (T4) and **triiodothyronine** (T3) (Ka1 .gtoreq.109M-1), as well as weak saturable T3 sites (Ka2 .apprx.108M-1). TBPA capacity for T4 is only Ka2 .apprx.108M-1 sites and for T3 only Ka1 .apprx.106M-1 sites. Consistent with these parameters are the specific responses of TBG and TBPA binding activities to varying serum concns. of T4, T3, **oleic** acid, diphenylhydrantoin (DPH), or salicylate. The primary attack of these compds. is at TBG. Small T4, oleate, or DPH doses chase the TBG-bound [125I]T4 to TBPA; high doses of T4 or oleate but not of DPH inhibit the [125I]T4

binding to both proteins. In the T3-serum interactions, all tested compds. displace the TBG-bound hormone without chasing it to TBPA. The high reactivity of TBG sites indicates the protein is involved in modulating the free vs. bound serum levels of T4 and T3 against physiol. or pathol. variations of binding competitors.

IT **51-48-9**, **Thyroxine**, biological studies
6893-02-3, **Triiodothyronine**
RL: BIOL (Biological study)
(globulin and prealbumin of blood serum binding of)

IT **112-80-1**, **Oleic** acid, biological studies
RL: BIOL (Biological study)
(thyroid hormones binding by blood serum proteins response to)

L11 ANSWER 12 OF 20 CAPLUS COPYRIGHT 1998 ACS
AN 1989:128991 CAPLUS
DN 110:128991
TI Uptake of 3,5,3'-**triiodothyronine** by cultured rat hepatoma cells is inhibitable by nonbile acid cholephils, diphenylhydantoin, and nonsteroidal antiinflammatory drugs
AU Topliss, Duncan J.; Kolliniatis, Emily; Barlow, John W.; Lim, Chen Fee; Stockigt, Jan R.
CS Dep. Med., Monash Univ., Melbourne, 3181, Australia
SO Endocrinology (Baltimore) (1989), 124(2), 980-6
CODEN: ENDOAO; ISSN: 0013-7227
DT Journal
LA English
AB Cellular uptake of T3 was examd. using rat H4 hepatoma cells. Uptake of [125I]T3 (10-11M) from serum-free medium was measured as the cell-assocd. counts retained by washed cells (2 .times. 106 per well). Displaceable uptake was 84% of total uptake at 2 min (2.9% of total counts). T4, tetraiodothyroacetic acid, triiodothyroacetic acid, rT3, and D-T3 were 2-5% as effective as T3 in displacing uptake. Nonequil. kinetics indicated a half-max. uptake at 680 nM T3 with .apprx.7 million sites/cell. Displaceable uptake was time and temp. dependent and was 73% inhibited by 2 mM KCN and 52% by 10 mM bacitracin but not by 2 mM ouabain or 10 .mu.M cytochalasin B. Phloretin, 100 .mu.M, inhibited uptake by 66%. T3 uptake was directly related to the free T3 concn. over the range of albumin concns., 0-10 g/L. The nonbile acid cholephil compds., bromosulfophthalein, iopanoic acid, and indocyanine green (all 100 .mu.M) inhibited T3 uptake to 62, 17, and 5% of control, resp. Taurocholate, methylaminoisobutyric acid, and **oleic** acid were noninhibitory. The half-inhibitory concns. of reactive nonsteroidal antiinflammatory drugs were: meclofenamic acid (25 .mu.M), mefanamic acid (45 .mu.M), fenclofenac (69 .mu.M), flufenamic acid (100 .mu.M), and diclofenac (230 .mu.M). Aspirin, ibuprofen, oxyphenbutazone, and phenylbutazone (all 100 .mu.M) were noninhibitory. Diphenylhydantoin inhibited uptake to 50% at 75 .mu.M. Apparently, T3 uptake by cultured rat hepatocytes is by an

energy-dependent, saturable, stereo-selective mechanism that is dependent on cell membrane proteins. This mechanism appears to be shared by a no. of other **ligands**, including nonbile acid cholephils and several nonsteroidal antiinflammatory drugs of the anthranilic acid phenylacetic acid classes, as well as diphenylhydantoin. The bile acid taurocholate, **oleic** acid, and a probe for type A amino acid uptake were inactive. The extent to which these effects may modify expression of thyroid hormone action remains to be established.

IT **51-48-9**, **Thyroxine**, biological studies
71-67-0, Bromosulfophthalein
RL: BIOL (Biological study)
(**triiodothyronine** uptake by liver inhibition by)

IT **6893-02-3**
RL: BIOL (Biological study)
(uptake of, by liver, regulation of)

L11 ANSWER 13 OF 20 CAPLUS COPYRIGHT 1998 ACS
AN 1987:436191 CAPLUS
DN 107:36191
TI Method for measuring free **ligands** in biological fluids
IN El Shami, A. Said
PA Diagnostic Products Corp., USA
SO Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 218309	A2	19870415	EP 86-300336	19860117
	EP 218309	A3	19880831		
	EP 218309	B1	19951115		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	EP 661540	A1	19950705	EP 95-103930	19860117
	EP 661540	B1	19980805		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	AT 130435	E	19951215	AT 86-300336	19860117
	AT 169410	E	19980815	AT 95-103930	19860117
	DK 8602196	A	19870405	DK 86-2196	19860512
	DK 169365	B1	19941010		
	AU 8657521	A1	19870409	AU 86-57521	19860516
	AU 602864	B2	19901101		
	ES 555425	A1	19870716	ES 86-555425	19860528
	CA 1299984	A1	19920505	CA 86-510762	19860604
	NO 8602278	A	19870406	NO 86-2278	19860606
	NO 168002	B	19910923		
	NO 168002	C	19920102		
	IL 79283	A1	19910630	IL 86-79283	19860630

	JP 62083666	A2	19870417	JP 86-157772	19860704
	JP 08001436	B4	19960110		
	FI 8603186	A	19870405	FI 86-3186	19860805
	FI 92878	B	19940930		
	FI 92878	C	19950110		
	JP 07311200	A2	19951128	JP 95-10194	19950125
	JP 2575338	B2	19970122		
PRAI	US 85-784857	19851004			
	EP 86-300336	19860117			

AB A method is described for measuring the concn. of a free **ligand** in biol. fluids in the presence of bound **ligand** and endogenous binding proteins, without disturbing the equil. between the free and the protein-bound **ligand**. The method comprises (1) incubating a sample with (i) a labeled **ligand** analog which does not bind to some of the endogenous binding proteins but does bind to .ltoreq.1 other endogenous binding protein, (ii) a specific **ligand** binder, and (iii) .gtoreq.1 specific inhibitor that inhibits the binding of the **ligand** analog to its endogenous binding protein; (2) sepg. the bound from the unbound **ligand** analog; and (3) detg. the concn. of the free **ligand** in the sample by comparing the bound fraction of the **ligand** analog to a calibration curve obtained using free **ligand** calibrators. Conditions for the detn. of T4 were worked out and comprise (1) using 125I-labeled N-L-thyroxinesuccinimide as the **ligand** analog (which binds to albumin, the endogenous binding protein, in the absence of inhibitors); (2) employing a 1:250,000 diln. of antibodies to T4 as the specific **ligand**, which has a lower affinity than albumin for the **ligand** analog; and (3) using 5 mg **Na salicylate**/mL as the inhibitor, which abolishes binding of the **ligand** analog to albumin and allows 49.2% binding of **ligand** analog to the antibodies.

IT **51-48-9**, **Thyroxine**, analysis **6893-02-3**
RL: ANST (Analytical study)
(detn. of free, in biol. fluids contg. endogenous receptor, **ligand** analog for)

IT **54-21-7**, **Sodium salicylate**
71-67-0, **Sulfobromophthalein 112-80-1**,
Oleic acid, biological studies
RL: ANST (Analytical study)
(**ligand** binding to endogenous receptor inhibition with, in free **ligand** detn. in biol. fluid contg. endogenous receptor)

IT **51-28-5**, biological studies
RL: BIOL (Biological study)
(**ligand** binding to endogenous receptor inhibition with, in free **ligand** detn. in biol. fluid contg. endogenous receptor)

L11 ANSWER 14 OF 20 CAPLUS COPYRIGHT 1998 ACS
AN 1986:65425 CAPLUS
DN 104:65425
TI Measuring free **ligand**
IN Buehler, Robert J.; Riceberg, Louis J.; Odstrchel, Gerald
PA Corning Glass Works, USA
SO Eur. Pat. Appl., 42 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 165669	A1	19851227	EP 85-302538	19850411
R: DE, FR, GB, IT				
JP 60249056	A2	19851209	JP 85-95323	19850502
CA 1305410	A1	19920721	CA 85-480717	19850503

PRAI US 84-607148 19840504
AB A single-step free **ligand** immunoassay is described. In this assay a blocking agent (e.g., salicylate) is included with labeled **ligand**. This blocking agent is present in an amt. which is sufficient to stop significant binding of the labeled **ligand** to various binding agents without causing significant release of bound **ligand**. For example, **thyroxine** was detd. in normal individuals and individuals with various diseases with and without **Na salicylate** (0.375 mg/mL) in the reaction mixt. The use of salicylate resulted in essentially the same values in normal individuals but with better precision. However, inclusion of **Na salicylate** provided diagnostically correct values in more patients.
IT **51-48-9**, analysis **6893-02-3**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, by specific binding assay, blocking agent effect on)
IT **54-21-7**
RL: ANST (Analytical study)
(in **thyroxine** detn., in blood serum of human by RIA)

L11 ANSWER 15 OF 20 CAPLUS COPYRIGHT 1998 ACS
AN 1986:29493 CAPLUS
DN 104:29493
TI Free analyte assay
IN Midgley, John Edward Maurice
PA Amersham International PLC, UK
SO Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	EP 155104	A2	19850918	EP 85-301212	19850222
	EP 155104	A3	19880727		
	R: DE, FR, GB, IT				
	JP 60194364	A2	19851002	JP 85-33656	19850221
PRAI	GB 84-4843		19840224		

AB A differential blocking agent is used to det. the free fraction of an analyte in a biol. fluid in the presence of protein-bound analyte. For example, free T4 was detd. with a com. RIA kit in which T4 competed with a labeled T4 deriv. for reaction with an immobilized antibody to T4. Addn. of 5-sulfosalicylic acid (5 .times. 10-5-5 .times. 10-2M) as differential blocking agent to the assay mixt. brought the free T4 values obtained into line with those expected from the clin. findings. Sulfosalicylic acid inhibited the binding of the labeled T4 deriv., but not of T4, to serum albumin.

IT **51-28-5**, biological studies **54-21-7**
RL: BIOL (Biological study)
(as differential blocking agent, in **thyroxine** detn. by RIA)

IT **51-48-9**, analysis
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, by RIA, sulfosalicylate in)

IT **112-80-1**, biological studies
RL: BIOL (Biological study)
(interference by, in **thyroxine** detn. in blood serum, sulfosalicylate effect on)

L11 ANSWER 16 OF 20 CAPLUS COPYRIGHT 1998 ACS
AN 1985:161168 CAPLUS
DN 102:161168
TI Free **ligand** assay
IN Ekins, Roger Philip; Jackson, Thomas Michael
PA UK
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8500226	A1	19850117	WO 84-GB220	19840622
	W: JP, US				
	RW: AT, BE, CH, DE, FR, GB, LU, NL, SE				
	EP 149631	A1	19850731	EP 84-902530	19840622
	EP 149631	B1	19881123		
	R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE				
	JP 60501674	T2	19851003	JP 84-502539	19840622
	JP 06019347	B4	19940316		
	CA 1227425	A1	19870929	CA 84-457231	19840622

	AT 38903	E	19881215	AT 84-902530	19840622
	US 4745072	A	19880517	US 85-705421	19850220
PRAI	GB 83-17124	19830623			
	EP 84-902530	19840622			
	WO 84-GB220	19840622			

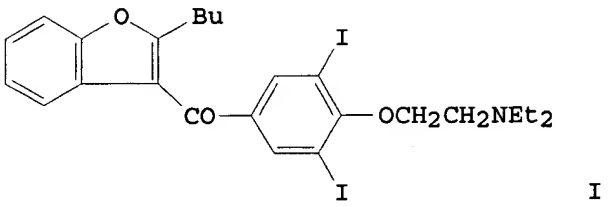
AB A method for measuring the concn. of a free **ligand** (such as thyroid hormones and other hormones) in a biol. fluid contg. the free **ligand** and **ligand** bound to an endogenous binding agent is devised by (1) mixing a fluid sample with an analog of the **ligand**, a specific binder with which the free **ligand** and analog bind, and an exogenous binding agent which binds only the analog, with either the **ligand** or the specific binder being labeled; (2) incubating the resulting mixt. so that the **ligand** and analog compete for the specific binder; (3) detg. either the amt. of the labeled analog bound to the specific binder or the exogenous binding agent or the amt. of labeled specific binder bound, or not bound, to the **ligand** analog; and (4) correlating the detd. amt. to the amt. of free **ligand** present in the sample. Thus, an analog of T4 [**51-48-9**] suitable for the immunoassay of free T4 was prepd., and an antibody against this analog was produced. The analog was then radiolabeled with 125I. A specific antibody against T4 with an equal affinity for the T4 analog was coupled to solid particles. A mixt. was prepd. of 0.5 mL of a suspension of the solid-phase antibody reagent, 0.5 mL of the [125I]T4 analog (2 nM), and 100 .mu.L of normal human serum. The extent of binding of the [125I]T4 analog to the specific binding reagent was correlated with the free T4 concn. A sample contg. 20 pM free T4 and 3 nM **oleic** acid [**112-80-1**] would be interpreted as contg. 10.6 pM free T4, a bias of 47%. When the binding agent for the analog was added, a sample contg. 20 pg free T4/mL and 1 mM **oleic** acid would be interpreted as contg. 17 pg free T4/mL, a neg. bias of only 15%.

IT **51-48-9**, analysis **51-48-9D**, analogs
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, by immunoassay)

IT **112-80-1**, uses and miscellaneous
RL: USES (Uses)
(**thyroxine** detn. by immunoassay in presence of)

L11 ANSWER 17 OF 20 CAPLUS COPYRIGHT 1998 ACS
AN 1984:583473 CAPLUS
DN 101:183473
TI Binding of amiodarone by serum proteins and the effects of drugs, hormones and other interacting **ligands**
AU Lalloz, M. R. A.; Byfield, P. G. H.; Greenwood, R. M.; Himsworth, R. L.
CS Endocrinol. Res. Group, Clin. Res. Cent., Harrow, HA1 3UJ, UK
SO J. Pharm. Pharmacol. (1984), 36(6), 366-72 .

CODEN: JPPMAB; ISSN: 0022-3573
DT Journal
LA English
GI



I

AB Amiodarone (I) [1951-25-3] is chiefly bound to albumin (62.1%) and much of the remainder (33.5%) is carried on a high mol. wt. protein, probably .beta.-lipoprotein. Anal. of data for amiodarone binding to albumin revealed a high affinity primary binding site (Ka 5.6 .times. 106 L mol-1) with about 4 secondary sites (av. Ka 1.9 .times. 103 L mol-1). Studies of the binding of amiodarone in serum revealed 1 type of binding site only with an affinity const. (Ka 4.2 .times. 106 L mol-1) similar to that of the primary site on albumin. The secondary albumin binding sites do not seem therefore to be utilized in whole serum and the affinity of the lipoprotein must be similar to that of the primary amiodarone binding site on albumin. The effects of a wide range of compds. on albumin binding of amiodarone were examd. by equil. dialysis to investigate if the known drug interactions of amiodarone are due to its serum protein binding properties. Amiodarone had no influence on the distribution of iodothyronines amongst their binding proteins nor were the concn. or binding properties of these proteins altered after prolonged treatment with the drug. Thus, altered iodothyronine concns. in amiodarone-treated patients cannot be attributed even in part to effects at the serum binding protein level.

IT **51-48-9**, biological studies **71-67-0**
RL: BIOL (Biological study)
(amiodarone binding by serum proteins response to, drug-drug interactions in relation to)

L11 ANSWER 18 OF 20 CAPLUS COPYRIGHT 1998 ACS
AN 1975:492681 CAPLUS
DN 83:92681
TI Z-fraction. I. Isolation and partial characterization of low molecular weight **ligand**-binding protein from rat hepatic cytosol
AU Warner, Margaret; Neims, Allen H.
CS Dep. Pharmacol. Ther., McGill Univ., Montreal, Que., Can.
SO Can. J. Physiol. Pharmacol. (1975), 53(3), 493-500

CODEN: CJPPA3
DT Journal
LA English
AB The Z-fraction was defined operationally as a **ligand**-binding (bilirubin **sulfobromophthalein**) portion of rat hepatic cytosol that eluted in the mol.-wt. region of 104 daltons after gel filtration. Polyacrylamide gel electrophoreses under different conditions, as well as binding stoichiometry, confirmed the anticipated heterogeneity of the Z-fraction. Three factors contributed to the subsequent resolution of the Z-fraction and partial characterization of that protein within the fraction with **ligand**-binding properties (Z-protein): (1) the use of hexachlorophene as **ligand**; (2) the inclusion of 20% glycerol during isolation to prevent aggregation and loss of binding activity; and (3) the development of a charcoal-binding assay. On ion-exchange chromatog., the Z-fraction resolved into a group of distinct protein components and an unidentified material with a high 260/280 nm absorbancy ratio. The 1 protein component with binding capacity exhibited homogeneity on polyacrylamide gel electrophoresis. Using the charcoal method, the apparent dissocn. consts. for the interaction between Z-protein and hexachlorophene, bilirubin, and L-**thyroxine**, were 20, 50, and 350.mu.M, resp. The Scatchard plot generated on extrapolation an n value of 1.0 with assumption of a mol. wt. for Z-protein of 104 daltons.
IT **51-48-9**, biological studies
RL: BIOL (Biological study)
(Z protein binding of)

L11 ANSWER 19 OF 20 CAPLUS COPYRIGHT 1998 ACS
AN 1975:423803 CAPLUS
DN 83:23803
TI Interactions of bilirubin and other **ligands** with ligandin
AU Kamisaka, Kazuaki; Listowsky, Irving; Gatmaitan, Zenaida; Arias, Irwin M.
CS Liver Res. Cent., Albert Einstein Coll. Med., Bronx, N. Y., USA
SO Biochemistry (1975), 14(10), 2175-80
CODEN: BICHAW
DT Journal
LA English
AB CD methods were used to study the structure of rat ligandin and the binding of org. anions to the protein. Ligandin has a highly ordered secondary structure with .apprx.40% .alpha. helix, 15% .beta. structure, and 45% random coil. Bilirubin binding occurred primarily at a single high-affinity site on the protein. The binding const. for bilirubin (5 .times. 107M-1) was highest among the **ligands** studied. The bilirubin-ligandin complex exhibited a well-defined CD spectrum with 2 major overlapping ellipticity bands of opposite sign in the bilirubin absorption region. This spectrum was virtually a mirror image of that of human

or rat serum albumin-bilirubin complexes. Studies on the direct transfer of bilirubin from ligandin to rat serum albumin showed that assocn. consts. of bilirubin-ligandin complexes were approx. 10-fold less than those of the bilirubin-albumin system. Ligandin exhibited a broad specificity with respect to the type of **ligand** bound. A series of org. anions including dyes used clin. for liver function tests, fatty acids, hormones, heme derivs., bile acids, and other **ligands** that were considered likely to interact with ligandin, were examd. Most induced ellipticity changes consistent with competitive displacement of bilirubin from ligandin and relative affinities of these compds. for ligandin were detd. based on their effectiveness in displacing the bilirubin. Some substances such as glutathione, conjugated **sulfobromophthaleins**, and lithocholic acid bound to ligandin but induced anomalous spectral shifts, when added to ligandin-bilirubin complexes. Other compds., including some that act as substrates for the glutathione transferase activity exhibited by ligandin, revealed no apparent competitive effects with respect to the bilirubin binding site.

IT **51-48-9**, biological studies **112-80-1**, biological studies **6893-02-3**
RL: PROC (Process)
(ligandin of liver binding of)

L11 ANSWER 20 OF 20 CAPLUS COPYRIGHT 1998 ACS
AN 1975:12601 CAPLUS
DN 82:12601
TI Protein binding of small molecules. IV. Relation between binding of phenolsulfophthalein dyes and other **ligands** with a high affinity for human serum albumin
AU Kragh-Hansen, U.; Moeller, J. V.; Lind, K. E.
CS Inst. Med. Biochem., Univ. Aarhus, Aarhus, Den.
SO Biochim. Biophys. Acta (1974), 365(2), 360-71
CODEN: BBACAQ
DT Journal
LA English
AB Binding of phenolsulfophthalein (phenol red) by human serum albumin was compared with binding of bromphenol blue and a variety of other high-affinity **ligands**. Phenol red and bromphenol blue were bound with a high affinity by serum albumin at 5 common sites. The assocn. consts. of these sites differed widely and were .apprx.100- to 1000-fold smaller for phenol red than for bromphenol blue. 1-Anilino-8-naphthalenesulfonate (ANS), dodecyl sulfate, and dodecylsulfonate displaced phenol red competitively from the high affinity sites of serum albumin. Dodecyl sulfate and dodecylsulfonate were less effective inhibitors of dye binding than ANS which competed with phenol red at 4-5 sites. On the other hand, bilirubin inhibited phenol red binding in more than stoichiometric amts., whereas L-**thyroxine** did not affect dye binding. Serum albumin defatted by charcoal treatment bound more phenol red

than native serum albumin. However, palmitate and oleate had only a modest inhibitory effect on phenol red binding, the fatty acids not being effective at binding levels < 4. Thus, common binding sites exist for phenolsulfophthalein dyes, ANS, and bilirubin, whereas fatty acids and L-**thyroxine** predominantly are bound at other locations on the albumin mol.

IT **51-48-9**, biological studies **112-80-1**, biological studies
RL: BIOL (Biological study)
(albumins of blood serum binding of, **ligands** in relation to)

=> d his l12

FILE 'USPATFULL' ENTERED AT 11:08:46 ON 23 DEC 1998
L12 37 S L11

=> d 1-37 .bevpat

L12 ANSWER 1 OF 37 USPATFULL
AN 1998:157163 USPATFULL
TI Mammalian multipotent neural stem cells
IN Anderson, David J., Altadena, CA, United States
Stemple, Derek L., Newton, MA, United States
PA California Institute of Technology, Pasadena, CA, United States (U.S. corporation)
PI US 5849553 981215
AI US 95-485612 950607 (8)
RLI Continuation-in-part of Ser. No. US 94-188286, filed on 28 Jan 1994, now patented, Pat. No. US 5654183 which is a continuation-in-part of Ser. No. US 92-969088, filed on 29 Oct 1992, now abandoned which is a continuation-in-part of Ser. No. US 92-920617, filed on 27 Jul 1992, now abandoned
DT Utility
EXNAM Primary Examiner: LeGuyader, John I.
LREP Flehr Hohbach Test Albritton & Herbert LLP; Trecartin, Richard F.; Silva, Robin M.
CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN 111 Drawing Figure(s); 44 Drawing Page(s)
LN.CNT 3072
AB The invention includes mammalian multipotent neural stem cells and their progeny and methods for the isolation and clonal propagation of such cells. At the clonal level the stem cells are capable of self regeneration and asymmetrical division. Lineage restriction is demonstrated within developing clones which are sensitive to the local environment. The invention also includes such cells which are transfected with foreign nucleic acid, e.g., to produce an immortalized neural stem cell, and immortalized cell lines

which are capable of subsequent disimmortalization. The invention further includes transplantation assays which allow for the identification of mammalian multipotent neural stem cells from various tissues and methods for transplanting mammalian neural stem cells and/or neural or glial progenitors into mammals. A novel method for detecting antibodies to neural cell surface markers is disclosed as well as a monoclonal antibody to mouse LNGFR.

INCL INCLM: 435/172.300
INCLS: 435/069.100; 435/320.100; 435/325.000; 435/353.000
NCL NCLM: 435/172.300
NCLS: 435/069.100; 435/320.100; 435/325.000; 435/353.000

L12 ANSWER 2 OF 37 USPATFULL
AN 1998:131759 USPATFULL
TI Stimulating the differentiation of predipocytic cells and therapies based thereon
IN Ailhaud, Gerald, Nice, France
Grimaldi, Paul, Nice, France
Safonova, Irina, Nice, France
Shroot, Braham, Antibes, France
Reichert, Uwe, Pont du Loup, France
PA Centre International De Recherches Dermatologiques Galderma, Valbonne, France (non-U.S. corporation)
PI US 5827897 981027
AI US 97-787216 970122 (8)
RLI Division of Ser. No. US 95-510312, filed on 2 Aug 1995, now patented, Pat. No. US 5728739
PRAI FR 94-9584 940802
DT Utility
EXNAM Primary Examiner: Weddington, Kevin E.
LREP Burns, Doane, Swecker & Mathis, L.L.P.
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 624
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The differentiation of preadipocytic cells into adipocytic cells, in particular for correcting insulin-resistance disease states in mammalian organisms, notably in humans, for example type II diabetes and cardiovascular disorders such as hypertension and atherosclerosis, is stimulated by treating such preadipocytic cells, or a patient in need of such treatment, with an effective amount of (a) at least one **ligand** displaying affinity for the nuclear receptors for retinoic acid and/or isomers thereof, preferably at least one **ligand** displaying a specific affinity for the RAR receptors and even more preferably the RAR-.alpha. receptor and (b) at least one fatty acid, e.g., a

polyunsaturated fatty acid.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/725.000
INCLS: 514/530.000; 514/549.000; 514/557.000; 514/558.000; 514/560.000
NCL NCLM: 514/725.000
NCLS: 514/530.000; 514/549.000; 514/557.000; 514/558.000; 514/560.000

L12 ANSWER 3 OF 37 USPATFULL
AN 1998:54875 USPATFULL
TI Intercellular adhesion mediators
IN Paulson, James C., Sherman Oaks, CA, United States
Perez, Mary S., Carlsbad, CA, United States
Gaeta, Federico C. A., La Jolla, CA, United States
Ratcliffe, Robert M., Carlsbad, CA, United States
PA Cytel Corporation, San Diego, CA, United States (U.S. corporation)
PI US 5753631 980519
AI US 95-457886 950531 (8)
RLI Division of Ser. No. US 93-63181, filed on 14 May 1993 which is a continuation-in-part of Ser. No. US 91-810789, filed on 17 Dec 1991, now abandoned which is a continuation-in-part of Ser. No. US 91-716735, filed on 17 Jun 1991, now abandoned which is a continuation-in-part of Ser. No. US 90-632390, filed on 21 Dec 1990, now abandoned which is a continuation-in-part of Ser. No. US 90-619319, filed on 28 Nov 1990, now abandoned which is a continuation-in-part of Ser. No. US 90-538853, filed on 15 Jun 1990, now abandoned
DT Utility
EXNAM Primary Examiner: Fonda, Kathleen K.
LREP Townsend and Townsend and Crew LLP
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 41 Drawing Figure(s); 24 Drawing Page(s)
LN.CNT 4107
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed towards compositions and methods for reducing or controlling inflammation and for treating inflammatory disease processes and other pathological conditions mediated by intercellular adhesion. The compositions of the invention include compounds that selectively bind selectin receptors, the selectin binding activity being mediated by a carbohydrate moiety. The selectin-binding moieties of the invention are derivatives of a sialylated, fucosylated N-acetyllactosamine unit of the Lewis X antigen. Compounds containing a selectin-binding moiety in both monovalent and multivalent forms are included in the invention. The compounds of the invention are provided as pharmaceutical compositions which

include, for example, liposomes that carry selectin-binding moieties of the invention. The invention further includes immunoglobulins capable of selectively binding an oligosaccharide **ligand** that is recognized by a selectin receptor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 514/025.000
INCLS: 514/008.000; 514/054.000; 514/061.000; 514/062.000; 536/017.200; 536/018.200; 536/018.700; 536/053.000; 536/054.000; 536/055.000; 536/055.100; 536/055.200

NCL NCLM: 514/025.000
NCLS: 514/008.000; 514/054.000; 514/061.000; 514/062.000; 536/017.200; 536/018.200; 536/018.700; 536/053.000; 536/054.000; 536/055.000; 536/055.100; 536/055.200

L12 ANSWER 4 OF 37 USPATFULL
AN 1998:28118 USPATFULL
TI Stimulating the differentiation of preadipocytic cells and therapies based thereon
IN Ailhaud, Gerard, Nice, France
Grimaldi, Paul, Nice, France
Safonova, Irina, Nice, France
Shroot, Braham, Antibes, France
Reichert, Uwe, Pont Du Loup, France
PA Centre International De Recherches Dermatologiques Galderma, Valbonne, France (non-U.S. corporation)
PI US 5728739 980317
AI US 95-510312 950802 (8)
PRAI FR 94-9584 940802
DT Utility
EXNAM Primary Examiner: Weddington, Kevin E.
LREP Burns, Doane, Swecker & Mathis, L.L.P.
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 588
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The differentiation of preadipocytic cells into adipocytic cells, in particular for correcting insulin-resistance disease states in mammalian organisms, notably in humans, for example type II diabetes and cardiovascular disorders such as hypertension and atherosclerosis, is stimulated by treating such preadipocytic cells, or a patient in need of such treatment, with an effective amount of (a) at least one **ligand** displaying affinity for the nuclear receptors for retinoic acid and/or isomers thereof, preferably at least one **ligand** displaying a specific affinity for the RAR receptors and even more preferably the RAR-.alpha. receptor and (b) at least one fatty acid, e.g., a polyunsaturated fatty acid.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/725.000
INCLS: 514/546.000; 514/547.000; 514/558.000; 514/559.000; 514/560.000
NCL NCLM: 514/725.000
NCLS: 514/546.000; 514/547.000; 514/558.000; 514/559.000; 514/560.000

L12 ANSWER 5 OF 37 USPATFULL
AN 1998:22068 USPATFULL
TI Immunological detection using two detectable labels
IN Abuknesha, Ramadan Arbi, London, United Kingdom
PA GEC-Marconi Limited, Stanmore, United Kingdom (non-U.S. corporation)
PI US 5723304 980303
WO 9403811 940217
AI US 95-381826 950227 (8)
WO 93-GB1628 930802
950227 PCT 371 date
950227 PCT 102(e) date
PRAI GB 92-16465 920803
GB 92-19743 920918
GB 92-20722 921001
GB 92-21578 921014
GB 92-24897 921127
GB 92-24898 921127
DT Utility
EXNAM Primary Examiner: Huff, Sheela
LREP Kirschstein, Ottinger, Israel & Schiffmiller, P.C.
CLMN Number of Claims: 31
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1823
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to a method of detection, a sensor and a test-kit which find application in immunological detection (e.g., immunoassay). The invention provides, inter alia, a method of detection, suitable for use in immunological detection of an entity, which method includes the use of a secondary species (as defined in the specification), the use of a first detectable species, and the use of a second detectable species. The method may include, for example, the use of a primary species, a secondary species, a first detectable species and a second detectable species. The primary species may be, for example, an antibody or a **ligand**. The secondary species may be, for example, an auxiliary species such as an auxiliary binder or an auxiliary **ligand**, or a species which has a part which is an auxiliary function. The entity to be detected may be an analyte

species as such or may be an entity which carries or includes analytes species.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/007.900
INCLS: 435/007.100; 435/007.200; 435/007.500; 435/007.910; 435/007.920; 435/007.930; 435/007.940; 435/007.950; 435/040.500; 435/174.000; 435/175.000; 435/176.000; 435/177.000; 435/178.000; 435/179.000; 435/180.000; 435/181.000; 435/960.000; 435/972.000; 436/518.000; 436/523.000; 436/524.000; 436/527.000; 436/528.000; 436/529.000; 436/530.000; 436/531.000; 436/532.000; 436/533.000; 436/534.000; 436/536.000
NCL NCLM: 435/007.900
NCLS: 435/007.100; 435/007.200; 435/007.500; 435/007.910; 435/007.920; 435/007.930; 435/007.940; 435/007.950; 435/040.500; 435/174.000; 435/175.000; 435/176.000; 435/177.000; 435/178.000; 435/179.000; 435/180.000; 435/181.000; 435/960.000; 435/972.000; 436/518.000; 436/523.000; 436/524.000; 436/527.000; 436/528.000; 436/529.000; 436/530.000; 436/531.000; 436/532.000; 436/533.000; 436/534.000; 436/536.000

L12 ANSWER 6 OF 37 USPATFULL
AN 97:112318 USPATFULL
TI Neural chest stem cell assay
IN Anderson, David J., Altadena, CA, United States
Stemple, Derek L., Newton, MA, United States
PA California Institute of Technology, Pasadena, CA, United States (U.S. corporation)
PI US 5693482 971202
AI US 95-474506 950607 (8)
RLI Division of Ser. No. US 94-188286, filed on 28 Jan 1994 which is a continuation-in-part of Ser. No. US 92-969088, filed on 29 Oct 1992, now abandoned which is a continuation-in-part of Ser. No. US 92-920617, filed on 27 Jul 1992, now abandoned
DT Utility
EXNAM Primary Examiner: LeGuyader, John L.
LREP Flehr Hohbach Test Albritton Herbert LLP; Trecartin, Richard F.; Silva, Robin M.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 62 Drawing Figure(s); 23 Drawing Page(s)
LN.CNT 2114
AB The invention includes mammalian multipotent neural stem cells and their progeny and methods for the isolation and clonal propagation of such cells. At the clonal level the stem cells are capable of self regeneration and asymmetrical division. Lineage restriction is demonstrated within developing clones which are sensitive to

the local environment. The invention also includes such cells which are transfected with foreign nucleic acid, e.g., to produce an immortalized neural stem cell. The invention further includes transplantation assays which allow for the identification of mammalian multipotent neural stem cells from various tissues and methods for transplanting mammalian neural stem cells and/or neural or glial progenitors into mammals. A novel method for detecting antibodies to neural cell surface markers is disclosed as well as a monoclonal antibody to mouse LNGFR.

INCL INCLM: 435/029.000
INCLS: 435/240.200
NCL NCLM: 435/029.000

L12 ANSWER 7 OF 37 USPATFULL
AN 97:88884 USPATFULL
TI Immoralized neural crest stem cells and methods of making
IN Anderson, David J., Altadena, CA, United States
Stemple, Derek L., Newton, MA, United States
PA California Institute of Technology, Pasadena, CA, United States (U.S. corporation)
PI US 5672499 970930
AI US 95-478920 950607 (8)
RLI Division of Ser. No. US 94-188286, filed on 28 Jan 1994 which is a continuation-in-part of Ser. No. US 92-969088, filed on 29 Oct 1992, now abandoned which is a continuation-in-part of Ser. No. US 92-920617, filed on 27 Jul 1992, now abandoned
DT Utility
EXNAM Primary Examiner: Leguyader, John L.
LREP Flehr Hohbach Test Albritton Herbert LLP; Trecartin, Richard F.; Silva, Robin M.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1,2
DRWN 62 Drawing Figure(s); 23 Drawing Page(s)
LN.CNT 2112
AB The invention includes mammalian multipotent neural stem cells and their progeny and methods for the isolation and clonal propagation of such cells. At the clonal level the stem cells are capable of self regeneration and asymmetrical division. Lineage restriction is demonstrated within developing clones which are sensitive to the local environment. The invention also includes such cells which are transfected with foreign nucleic acid, e.g., to produce an immortalized neural stem cell. The invention further includes transplantation assays which allow for the identification of mammalian multipotent neural stem cells from various tissues and methods for transplanting mammalian neural stem cells and/or neural or glial progenitors into mammals. A novel method for detecting antibodies to neural cell surface markers is disclosed as well as a monoclonal antibody to mouse LNGFR.

INCL INCLM: 435/240.400
INCLS: 435/069.100; 435/172.300; 435/320.100
NCLS: 435/069.100; 435/320.100; 435/325.000; 435/353.000; 435/368.000; 435/467.000

L12 ANSWER 8 OF 37 USPATFULL
AN 97:68355 USPATFULL
TI Genetically engineered mammalian neural crest stem cells
IN Anderson, David J., Altadena, CA, United States
Stemple, Derek L., Newton, MA, United States
PA California Institute of Technology, Pasadena, CA, United States (U.S. corporation)
PI US 5654183 970805
AI US 94-188286 940128 (8)
RLI Continuation-in-part of Ser. No. US 92-996088, filed on 23 Dec 1992, now patented, Pat. No. US 5365699 which is a continuation-in-part of Ser. No. US 92-920617, filed on 27 Jul 1992, now abandoned
DT Utility
EXNAM Primary Examiner: LeGuyader, John L.
LREP Flehr, Hohbach, Test, Albritton & Herbert
CLMN Number of Claims: 17
ECL Exemplary Claim: 1,4
DRWN 62 Drawing Figure(s); 23 Drawing Page(s)
LN.CNT 2162
AB The invention includes mammalian multipotent neural stem cells and their progeny and methods for the isolation and clonal propagation of such cells. At the clonal level the stem cells are capable of self regeneration and asymmetrical division. Lineage restriction is demonstrated within developing clones which are sensitive to the local environment. The invention also includes such cells which are transfected with foreign nucleic acid, e.g., to produce an immortalized neural stem cell. The invention further includes transplantation assays which allow for the identification of mammalian multipotent neural stem cells from various tissues and methods for transplanting mammalian neural stem cells and/or neural or glial progenitors into mammals. A novel method for detecting antibodies to neural cell surface markers is disclosed as well as a monoclonal antibody to mouse LNGFR.

INCL INCLM: 435/172.300
INCLS: 435/069.100; 435/320.100; 435/325.000; 435/353.000; 435/368.000
NCL NCLM: 435/456.000
NCLS: 435/069.100; 435/320.100; 435/325.000; 435/353.000; 435/368.000

L12 ANSWER 9 OF 37 USPATFULL

AN 97:51869 USPATFULL
TI Isolated nucleic acid encoding a ubiquitous nuclear receptor
IN Liao, Shutsung, Chicago, IL, United States
Song, Ching, Durham, NC, United States
PA Arch Development Corporation, Chicago, IL, United States (U.S. corporation)
PI US 5639616 970617
AI US 94-342411 941118 (8)
RLI Continuation-in-part of Ser. No. US 93-152003, filed on 10 Nov 1993, now abandoned
DT Utility
EXNAM Primary Examiner: Walsh, Stephen G.; Assistant Examiner: Ulm, John D.
LREP Arnold White & Durkee
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN 21 Drawing Figure(s); 18 Drawing Page(s)
LN.CNT 4472
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates generally to compositions of and methods for obtaining ubiquitous, nuclear receptor (UR) polypeptides. The invention also relates to polynucleotides encoding UR polypeptides, recombinant host cells and vectors containing UR-encoding polynucleotide sequences, and recombinant UR polypeptides. By way of example, the invention discloses the cloning and functional expression of at least two different UR polypeptides. The invention also includes methods for using the isolated, recombinant receptor polypeptides in assays designed to select substances which interact with UR polypeptides for use in diagnostic, drug design and therapeutic applications.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/007.100
INCLS: 435/069.100; 435/252.300; 435/320.100; 536/023.500; 536/024.300
NCL NCLM: 435/007.100
NCLS: 435/069.100; 435/252.300; 435/320.100; 536/023.500; 536/024.300

L12 ANSWER 10 OF 37 USPATFULL
AN 97:17918 USPATFULL
TI Compositions and methods for enhanced drug delivery
IN Hale, Ron L., Woodside, CA, United States
Lu, Amy, Los Altos, CA, United States
Solas, Dennis, San Francisco, CA, United States
Selick, Harold E., Belmont, CA, United States
Oldenburg, Kevin R., Fremont, CA, United States
Zaffaroni, Alejandro C., Atherton, CA, United States
PA Affymax Technologies N.V., Middlesex, England (non-U.S.

corporation)
PI US 5607691 970304
AI US 95-449188 950524 (8)
RLI Continuation of Ser. No. US 93-164293, filed on 9 Dec 1993, now abandoned which is a continuation-in-part of Ser. No. US 93-77296, filed on 14 Jun 1993, now abandoned which is a continuation-in-part of Ser. No. US 92-898219, filed on 12 Jun 1992, now abandoned And a continuation-in-part of Ser. No. US 93-9463, filed on 27 Jan 1993, now abandoned
DT Utility
EXNAM Primary Examiner: Levy, Neil S.
LREP Stevens, Lauren L.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5349
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to methods of delivering pharmaceutical agents across membranes, including the skin layer or mucosal membranes of a patient. A pharmaceutical agent is covalently bonded to a chemical modifier, via a physiologically cleavable bond, such that the membrane transport and delivery of the agent is enhanced.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/449.000
INCLS: 604/020.000; 514/001.000; 514/002.000; 514/026.000; 514/183.000; 514/169.000; 514/553.000; 514/556.000
NCL NCLM: 424/449.000
NCLS: 514/001.000; 514/002.000; 514/026.000; 514/169.000; 514/183.000; 514/553.000; 514/556.000; 604/020.000

L12 ANSWER 11 OF 37 USPATFULL
AN 97:14683 USPATFULL
TI Sialyl Le.sup.x analogues as inhibitors of cellular adhesion
IN DeFrees, Shawn A., San Marcos, CA, United States
Gaeta, Federico C. A., Olivenhain, CA, United States
Gaudino, John J., Westlake Village, CA, United States
Zheng, Zhongli, Lexington, MA, United States
Hayashi, Masaji, Kobe, Japan
PA Cytel Corporation, San Diego, CA, United States (U.S. corporation)
PI US 5604207 970218
AI US 94-345072 941128 (8)
RLI Continuation-in-part of Ser. No. US 94-241645, filed on 12 May 1994 which is a continuation-in-part of Ser. No. US 93-62120, filed on 14 May 1993, now abandoned
DT Utility
EXNAM Primary Examiner: Kunz, Gary L.; Assistant Examiner: Fonda, Kathleen Kahler

LREP Townsend and Townsend and Crew
CLMN Number of Claims: 44
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3352
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The inventive compounds are analogues of sialyl Le.sup.x that inhibit cellular adhesion between a selectin and cells that express sialyl Le.sup.x on their surfaces, and their synthetic intermediates. An inventive compound has structure A, ##STR1## wherein Z is hydrogen, C.sub.1 -C.sub.6 acyl or ##STR2## Y is C(O), SO.sub.2, HNC(O), OC(O) or SC(O); R.sup.1 is an aryl, a substituted aryl or a phenyl C.sub.1 -C.sub.3 alkylene group, wherein an aryl group has one five- or six-membered aromatic ring, a fused five/six-membered aromatic ring, or two fused six-membered aromatic rings, which rings are hydrocarbyl, monooxahydrocarbyl, monothiahydrocarbyl, monoazahydrocarbyl or diazahydrocarbyl rings, and a substituted aryl group is an aryl group having a halo, trifluoromethyl, nitro, C.sub.1 -C.sub.18 alkyl, C.sub.1 -C.sub.18 alkoxy, amino, mono-C.sub.1 -C.sub.18 alkylamino, di-C.sub.1 -C.sub.18 alkylamino, benzylamino, C.sub.1 -C.sub.18 alkylbenzylamino, C.sub.1 -C.sub.18 thioalkyl or C.sub.1 -C.sub.18 alkyl carboxamido substituent, or

R.sup.1 Y is allyloxycarbonyl or chloroacetyl;

R.sup.2 is hydrogen, C.sub.1 -C.sub.18 straight chain, branched chain or cyclic hydrocarbyl, C.sub.1 -C.sub.6 alkyl C.sub.1 -C.sub.5 alkylene .omega.-carboxylate, .omega.-tri(C.sub.1 -C.sub.4 alkyl/phenyl)silyl C.sub.2 -C.sub.4 alkylene, monosaccharide or disaccharide,

or OR.sup.2 together form a C.sub.1 -C.sub.18 straight chain, branched chain or cyclic hydrocarbyl carbamate;

R.sup.3 is hydrogen or C.sub.1 -C.sub.6 acyl;

R.sup.4 is hydrogen, C.sub.1 -C.sub.6 alkyl or benzyl;

R.sup.5 is hydrogen, benzyl, methoxybenzyl, dimethoxybenzyl or C.sub.1 -C.sub.6 acyl;

R.sup.7 is methyl or hydroxymethyl; and

X is C.sub.1 -C.sub.6 acyloxy, C.sub.2 -C.sub.6 hydroxylacyloxy, hydroxy, halo or azido.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/025.000

Searcher : Shears 308-4994

INCLS: 514/054.000; 514/061.000; 514/062.000; 536/017.200; 536/063.000; 536/064.000; 536/065.000; 536/055.000; 536/055.100; 536/055.200
NCL NCLM: 514/025.000
NCLS: 514/054.000; 514/061.000; 514/062.000; 536/017.200; 536/055.000; 536/055.100; 536/055.200; 536/063.000; 536/064.000; 536/065.000

L12 ANSWER 12 OF 37 USPATFULL
AN 96:87593 USPATFULL
TI Bivalent sialyl X saccharides
IN Gaeta, Federico C. A., Foster City, CA, United States
DeFrees, Shawn A., San Marcos, CA, United States
PA Cytel Corporation, San Diego, CA, United States (U.S. corporation)
PI US 5559103 960924
AI US 94-278020 940720 (8)
RLI Continuation-in-part of Ser. No. US 93-95657, filed on 21 Jul 1993, now abandoned
DT Utility
EXNAM Primary Examiner: Kunz, Gary L.; Assistant Examiner: Fonda, Kathleen Kahler
LREP Townsend and Townsend and Crew LLP
CLMN Number of Claims: 27
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 2363
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to bivalent sialyl Lewis X saccharide compounds that inhibit cellular binding to a selectin receptor. Pharmaceutical compositions containing a compound of Formula I, and processes for making and using the same are disclosed. A contemplated bivalent sialyl Lewis X saccharide compound has a structure that corresponds to Formula I, below, ##STR1## wherein R is a directly linked divalent monosaccharide unit; Y is selected from the group consisting of C(O), SO.sub.2, HNC(O), OC(O) and SC(O);

R.sup.2 is selected from the group consisting of a C.sub.1 -C.sub.6 hydrocarbyl, an aryl, a substituted aryl and a phenyl C.sub.1 -C.sub.3 alkylene group, wherein an aryl group has one six-membered aromatic ring or two fused six-membered aromatic rings, which ring or rings are hydrocarbyl, monoazahydrocarbyl, or diazahydrocarbyl rings, and a substituted aryl group is a before-mentioned aryl group having a substituent selected from the group consisting of halo, trifluoromethyl, nitro, C.sub.1 -C.sub.6 alkyl, C.sub.1 -C.sub.6 alkoxy, amino, mono-C.sub.1 -C.sub.6 alkylamino, di-C.sub.1 -C.sub.6 alkylamino, benzylamino and C.sub.1 -C.sub.6 alkylbenzylamino;

R.sup.3 is methyl or hydroxymethyl;

X is selected from the group consisting of hydroxyl, C.sub.1 -C.sub.6 acyloxy, C.sub.2 -C.sub.6 hydroxylacyloxy, halo and azido;

Z.sup.1 and Z.sup.2 are .alpha.-L-fucosyl or hydrogen (H), but at least one of Z.sup.1 and Z.sup.2 is .alpha.-L-fucosyl; and

M is a proton (H.sup.+) or a pharmaceutically acceptable cation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/054.000
INCLS: 514/062.000; 514/886.000; 514/887.000; 536/053.000; 536/054.000; 536/055.000; 536/055.100; 536/055.200; 530/395.000; 530/396.000
NCL NCLM: 514/054.000
NCLS: 514/062.000; 514/886.000; 514/887.000; 530/395.000; 530/396.000; 536/053.000; 536/054.000; 536/055.000; 536/055.100; 536/055.200

L12 ANSWER 13 OF 37 USPATFULL
AN 95:5872 USPATFULL
TI Method for the quantitative determination of a free form of substances present in biological fluids
IN Romelli, Pier B., Rho, Italy
Chiodoni, Giovanni, Vaprio d'Adda, Italy
Ringhini, Roberto, Cassina De' Pecchi, Italy
PA Technogenetics S.r.l., Milan, Italy (non-U.S. corporation)
PI US 5382530 950117
AI US 92-997735 921230 (7)
PRAI IT 92-910 920414
DT Utility
EXNAM Primary Examiner: Nucker, Christine M.; Assistant Examiner: Dubrule, Chris
LREP Darby & Darby
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 921
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed is a method for the direct determination of the free fraction of analytes present in biological fluids in a free form and in a form bound to one or more endogenous **ligands** (said free and bound forms being in equilibrium with one another). This method provides for a (preferably substantially simultaneous) use:a first **ligand** L1 capable of sequestering an analyte quantity proportionate to the free-analyte concentration present in a biological fluid and to subsequently release it, after

removal from the biological fluid of the specific endogenous **ligand**, as a result of the addition of an appropriate selective dissociating agent; a second **ligand** capable of binding both the previously released analyte and a labelled version of the analyte, even in the presence of the dissociating agent; a selective dissociating agent; and a quantity of labelled analyte. The measured level of the labelled analyte which binds to the second exogenous **ligand** (or which remains unbound) is used to determine the concentration of the free analyte in the fluid.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 436/500.000
INCLS: 436/518.000; 436/825.000; 435/007.920; 435/007.930
NCL NCLM: 436/500.000
NCLS: 435/007.920; 435/007.930; 436/518.000; 436/825.000

L12 ANSWER 14 OF 37 USPATFULL
AN 92:34053 USPATFULL
TI Use of oxidase enzyme systems in chemiluminescent assays
IN Baret, Alain, Lafayette, France
PA Canberra Industries, Inc., Meriden, CT, United States (U.S. corporation)
PI US 5108893 920428
AI US 90-536181 900611 (7)
RLI Continuation-in-part of Ser. No. US 87-81159, filed on 4 Aug 1987, now patented, Pat. No. US 4933276, issued on 12 Jun 1990
PRAI FR 86-11415 860806
DT Utility
EXNAM Primary Examiner: Kepplinger, Esther L.; Assistant Examiner: Wolski, Susan C.
LREP Arnold, White & Durkee
CLMN Number of Claims: 25
ECL Exemplary Claim: 17
DRWN 13 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 1018
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A xanthine oxidase enzyme system to provide long lived entities capable of being recognized by a chemiluminescent reagent is disclosed. In the examples provided, a specific binding pair **ligand** or analyte is coupled with xanthine oxidase, either directly or via a streptavidin bridge. Thereafter, the presence of an analyte can be determined by a chemiluminescent emission upon addition of a signal reagent comprising hypoxanthine, iron EDTA complex and luminol dissolved in barbital buffer. The resulting chemiluminescent signal is stable and detectable for many hours after initiation. The chemiluminescent xanthine oxidase system is particularly useful for immunoassays and DNA probe analysis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/006.000
INCLS: 435/025.000; 435/028.000; 435/810.000; 436/172.000; 252/700.000
NCL NCLM: 435/006.000
NCLS: 252/700.000; 435/025.000; 435/028.000; 435/810.000; 436/172.000

L12 ANSWER 15 OF 37 USPATFULL
AN 92:27432 USPATFULL
TI Method of gene mapping
IN Livak, Kenneth J., Wilmington, DE, United States
Brenner, Sydney, Cambridge, England
PA E. I. Du Pont de Nemours and Company, Wilmington, DE, United States (U.S. corporation)
PI US 5102785 920407
AI US 88-185741 880425 (7)
RLI Continuation-in-part of Ser. No. US 87-103105, filed on 28 Sep 1987, now abandoned
DT Utility
EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Zitomer, Stephanie W.
CLMN Number of Claims: 39
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 2926
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The method described characterizes each DNA segment to be mapped by cleaving it to produce DNA fragments which are then end labeled with a reporter(s) specific to the end nucleotides of each fragment. The labeled fragments are again cleaved to produce short fragments which are separated according to size. The short fragments are analyzed as to report identify and size which is indicative of the character of each fragment. By derivatizing the cleaved ends of the primary cleaved fragments, the labeling may be delayed until the second cleavage. Prior to the labeling the derivatized fragments, all underivatized fragments are removed, the derivatized fragments being immobilized.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/006.000
INCLS: 435/091.000; 536/026.000; 536/027.000; 536/028.000; 536/029.000; 436/094.000; 436/501.000; 935/077.000
NCL NCLM: 435/006.000
NCLS: 435/091.530; 436/094.000; 436/501.000

L12 ANSWER 16 OF 37 USPATFULL
AN 91:86794 USPATFULL
TI Affinity matrices of modified polysaccharide supports

IN Hou, Kenneth C., Glastonbury, CT, United States
Liao, Tung-Ping D., Missouri City, TX, United States
Rohan, Robert, Columbia, CT, United States
PA Cuno Inc., Meridan, CT, United States (U.S. corporation)
PI US 5059654 911022
AI US 89-311498 890216 (7)
RLI Continuation-in-part of Ser. No. US 88-154815, filed on 11 Feb 1988, now abandoned which is a continuation-in-part of Ser. No. US 87-130186, filed on 8 Dec 1987, now abandoned which is a continuation-in-part of Ser. No. US 87-13512, filed on 27 Jan 1987, now abandoned which is a continuation-in-part of Ser. No. US 84-656922, filed on 2 Oct 1984, now patented, Pat. No. US 4639513 which is a continuation-in-part of Ser. No. US 84-576448, filed on 2 Feb 1984, now patented, Pat. No. US 4663163 which is a continuation-in-part of Ser. No. US 83-466114, filed on 14 Feb 1983, now abandoned
DT Utility
EXNAM Primary Examiner: Nutter, Nathan M.
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN 34 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 3382
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention is directed to a modified polysaccharide material which comprises: (1) polysaccharide covalently bonded to a synthetic polymer; (2) the synthetic polymer being made from (a) a polymerizable compound which is capable of being covalently coupled directly or indirectly to said polysaccharide, and (b) one or more polymerizable compounds containing (i) a chemical group capable of causing the covalent coupling of the compound (b) to an affinity **ligand** or a biologically active molecule or (ii) a hydrophobic compound.

The invention is also directed to devices for the chromatographic separation of at least two components of a mixture comprising the modified polysaccharide material of the invention, wherein the device is configured for radial or tangential flow.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 525/054.100
INCLS: 525/054.200; 525/054.210; 530/412.000; 530/413.000; 210/656.000; 210/198.200; 210/502.100; 422/059.000; 422/070.000; 422/089.000; 435/091.000; 435/180.000
NCL NCLM: 525/054.100
NCLS: 210/198.200; 210/502.100; 210/656.000; 422/059.000; 422/070.000; 422/089.000; 435/180.000; 525/054.200; 525/054.210; 530/391.100; 530/391.500; 530/412.000; 530/413.000; 536/023.100

L12 ANSWER 17 OF 37 USPATFULL
AN 90:81738 USPATFULL
TI Fluorometric analysis method
IN Wieder, Irwin, 459 Panchita Way, Los Altos, CA, United States 94022
Wollenberg, Robert H., Los Altos, CA, United States
PA Wieder, Irwin, Los Altos, CA, United States (U.S. individual)
PI US 4965211 901023
AI US 83-550504 831109 (6)
RLI Continuation of Ser. No. US 81-260575, filed on 5 May 1981, now abandoned which is a division of Ser. No. US 79-73728, filed on 10 Sep 1979, now patented, Pat. No. US 4352751, issued on 5 Oct 1982
DT Utility
EXNAM Primary Examiner: Nucker, Christine M.; Assistant Examiner: Wallen, T. J.
LREP Fentress, S. B.; Flattery, P. C.; Hartenberger, R. E.
CLMN Number of Claims: 43
ECL Exemplary Claim: 30
DRWN No Drawings
LN.CNT 995
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Species-linked diamine triacetic acids of the formula ##STR1## wherein T is an organic species containing at least one amine, hydroxyl, or thiol functional group, L is the residue of at least one of those functional groups and R is a two or more atom long covalent bridge, are disclosed. Methods for their preparation, for the preparation of metal chelates from them and for the use of the chelates are also disclosed. In a preferred embodiment, the metal ions employed in the formation of the chelates are rare earth metal ions capable of forming fluorescent chelates which can in turn be employed in fluoroassay techniques.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 436/543.000
INCLS: 436/537.000; 436/547.000; 436/500.000; 436/501.000; 436/503.000; 436/513.000; 252/301.160; 252/301.170; 252/301.180; 556/001.000; 556/044.000; 556/050.000; 556/055.000; 556/063.000; 556/077.000; 556/107.000; 534/010.000; 560/169.000; 435/004.000; 435/007.000; 534/013.000; 534/016.000; 556/116.000; 556/134.000; 556/136.000; 556/148.000; 556/176.000; 556/137.000
NCL NCLM: 436/543.000
NCLS: 252/301.160; 252/301.170; 252/301.180; 435/004.000; 435/007.320; 435/007.400; 436/500.000; 436/501.000; 436/503.000; 436/513.000; 436/537.000; 436/546.000; 436/547.000; 534/010.000; 534/013.000; 534/016.000; 556/001.000; 556/044.000; 556/050.000; 556/055.000; 556/063.000; 556/077.000; 556/107.000; 556/116.000; 556/134.000; 556/136.000; 556/137.000; 556/148.000;

556/176.000; 560/169.000

L12 ANSWER 18 OF 37 USPATFULL
AN 90:1106 USPATFULL
TI Particle with luminescer for assays
IN Pease, John, Los Altos, CA, United States
Weng, Litai, Mountain View, CA, United States
Kirakossian, Hrair, San Jose, CA, United States
Ullman, Edwin F., Atherton, CA, United States
PA Syntex (U.S.A.) Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 4891324 900102
AI US 87-925 870107 (7)
DT Utility
EXNAM Primary Examiner: Benson, Robert
LREP Leitereg, Theodore J.; Barrett, Carole F.; Swiss, Gerald F.
CLMN Number of Claims: 56
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1663
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Assay methods are provided for determining an analyte in a sample suspected of containing the analyte. The method is carried out using a composition that includes a conjugate of a first sbp member with a particle. A luminescer is reversibly associated with a nonaqueous phase of the particle. Where the first sbp member is not complementary to the analyte, a second sbp member that is capable of binding to the first sbp member is employed. Unbound conjugate is separated from conjugate that is bound to the analyte or to the second sbp member. A reagent for enhancing the detectability of the luminescer is added and the light emission of the luminescer acted on by the reagent is measured.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 436/519.000
INCLS: 436/520.000; 436/522.000; 436/528.000; 436/533.000; 436/534.000; 436/535.000; 436/546.000; 436/800.000; 436/805.000; 436/808.000; 436/809.000; 436/821.000; 436/823.000; 436/829.000; 428/402.000
NCL NCLM: 436/519.000
NCLS: 428/402.000; 436/520.000; 436/522.000; 436/528.000; 436/533.000; 436/534.000; 436/535.000; 436/546.000; 436/800.000; 436/805.000; 436/808.000; 436/809.000; 436/821.000; 436/823.000; 436/829.000

L12 ANSWER 19 OF 37 USPATFULL
AN 89:7470 USPATFULL
TI Fluorescent labels having a polysaccharide bound to polymeric particles

IN Burdick, Brent A., Rochester, NY, United States
Danielson, Susan J., Rochester, NY, United States
PA Eastman Kodak Company, Rochester, NY, United States (U.S. corporation)
PI US 4801504 890131
AI US 87-100513 870924 (7)
RLI Division of Ser. No. US 85-713206, filed on 18 Mar 1985, now patented, Pat. No. US 4719182
DT Utility
EXNAM Primary Examiner: Warden, Robert J.; Assistant Examiner: Benson, Robert
LREP Tucker, J. Lanny
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 908
AB Fluorescent labels comprise a polysaccharide bound to a polymeric particle which contains a fluorescent rare earth chelate. These labels can be attached to any of a variety of physiologically reactive species to provide labeled species which have improved stability in aqueous solutions. The labeled species are particularly useful in specific binding assays to determine an immunologically reactive **ligand**, e.g. a hapten, in either solution or dry analytical techniques.

INCL INCLM: 428/403.000
INCLS: 436/529.000; 436/530.000; 436/533.000; 436/534.000; 436/546.000
NCL NCLM: 428/403.000
NCLS: 436/529.000; 436/530.000; 436/533.000; 436/534.000; 436/546.000

L12 ANSWER 20 OF 37 USPATFULL
AN 88:80602 USPATFULL
TI Homogenous specific binding assay reagent system and labeled conjugates
IN Boguslaski, Robert C., Elkhart, IN, United States
Carrico, Robert J., Bremen, IN, United States
Christner, James E., Ann Arbor, MI, United States
PA Miles Inc., Elkhart, IN, United States (U.S. corporation)
PI US 4791055 881213
AI US 86-817464 860109 (6)
DCD 20031216
RLI Division of Ser. No. US 78-894836, filed on 10 Apr 1978, now patented, Pat. No. US 4629688 which is a continuation of Ser. No. US 76-667996, filed on 18 Mar 1976, now abandoned which is a continuation-in-part of Ser. No. US 75-572008, filed on 28 Apr 1975, now abandoned
DT Utility

EXNAM Primary Examiner: Naff, David M.
LREP Klawitter, Andrew L.
CLMN Number of Claims: 38
ECL Exemplary Claim: 32
DRWN 12 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 2414
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The reactant advantageously is an enzymatic reactant such as an enzyme substrate or coenzyme. The activity of the conjugated reactant as a constituent of a predetermined reaction is affected by reaction between the specific binding substance in the conjugate and a specific binding counterpart thereto. The presence of a **ligand** in a liquid medium may be determined using competitive or displacement binding or sequential saturation techniques wherein the specific binding substance in the conjugate is the **ligand** or a specific binding analog thereof, or using a direct binding technique wherein the specific binding substance is a specific binding partner of the **ligand**. The effect of the specific binding reaction on the activity of the conjugated reactant is related to the presence or amount of the **ligand** in the liquid medium tested.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/007.000
INCLS: 435/174.000; 436/537.000; 436/544.000; 436/546.000
NCL NCLM: 435/007.700
NCLS: 435/007.720; 435/007.910; 435/174.000; 436/537.000; 436/544.000; 436/546.000

L12 ANSWER 21 OF 37 USPATFULL
AN 88:31018 USPATFULL
TI Immunoassay and immunometric assay of free **ligand** concentrations in biological fluids
IN Ekins, Roger P., Department of Molecular Endocrinology, The Middlesex Hospital School of Medicine, Mortimer Street, London, England
Jackson, Thomas M., Department of Molecular Endocrinology, The Middlesex Hospital School of Medicine, Mortimer Street, London, England W1N 8AA
PI US 4745072 880517
WO 8500226 850117
AI US 85-705421 850220 (6)
WO 84-GB220 840622
850220 PCT 371 date
850220 PCT 102(e) date
PRAI GB 83-17124 830623
DT Utility
EXNAM Primary Examiner: Marantz, Sidney
LREP Steele, Gould & Fried
Searcher : Shears 308-4994

CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 397
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of measuring the concentration of a free **ligand** in a biological fluid containing the free **ligand** and **ligand** bound to endogenous binding agent, by the steps of

(a) mixing a sample of the fluid with an analogue of the **ligand**, a specific binder with which the free **ligand** and the **ligand** analogue bind, and an exogenous binding agent which binds the **ligand** analogue but not the **ligand**, either the **ligand** analogue or the specific binder being labelled,

(b) incubating the resulting mixture,

(c) determining either the amount of the labelled analogue bound or the amount of labelled specific binder bound, or not bound, to the **ligand** analogue, and

(d) correlating the determined amount to the amount of free **ligand** present in the sample.

The method is useful to measure concentration of free thyroid hormones and other hormones in body fluids, employing antibodies specific to the **ligand** analogue as the exogenous binding agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 436/500.000
INCLS: 436/501.000; 436/534.000; 436/545.000; 436/804.000; 436/817.000
NCL NCLM: 436/500.000
NCLS: 436/501.000; 436/534.000; 436/545.000; 436/804.000; 436/817.000

L12 ANSWER 22 OF 37 USPATFULL
AN 88:2855 USPATFULL
TI Fluorescent labels and labeled species and their use in analytical elements and determinations
IN Burdick, Brent A., Rochester, NY, United States
Danielson, Susan J., Rochester, NY, United States
PA Eastman Kodak Company, Rochester, NY, United States (U.S. corporation)
PI US 4719182 880112
AI US 85-713206 850318 (6)
DT Utility

EXNAM Primary Examiner: Kepplinger, Esther M.; Assistant Examiner: Benson, Robert
LREP Tucker, J. Lanny
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1025
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Fluorescent labels comprise a polysaccharide bound to a polymeric particle which contains a fluorescent rare earth chelate. These labels can be attached to any of a variety of physiologically reactive species to provide labeled species which have improved stability in aqueous solutions. The labeled species are particularly useful in specific binding assays to determine an immunologically reactive **ligand**, e.g. a hapten, in either solution or dry analytical techniques.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 436/501.000
INCLS: 436/533.000; 436/534.000; 436/800.000; 436/546.000; 436/805.000; 436/808.000
NCL NCLM: 436/501.000
NCLS: 436/533.000; 436/534.000; 436/546.000; 436/800.000; 436/805.000; 436/808.000

L12 ANSWER 23 OF 37 USPATFULL
AN 87:79744 USPATFULL
TI Fluorescent chlorophyll labeled assay reagents
IN Hendrix, John L., Marietta, GA, United States
PA Bio-Diagnostics, Inc., Arlington, TX, United States (U.S. corporation)
PI US 4707454 871117
AI US 84-580875 840216 (6)
RLI Continuation-in-part of Ser. No. US 81-291793, filed on 10 Aug 1981
DT Utility
EXNAM Primary Examiner: Nucker, Christine M.; Assistant Examiner: Wieder, Stephen C.
LREP Jones, Askew & Lunsford
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 1153
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A fluora immuno assay system. A fluorescent labeled assay reagent is prepared by conjugating an assay reagent with a fluorescent labeling agent. The fluorescent labeling agent is a chlorophyll or a porphyrin having a Stokes shift of not less than 150 nanometers. Apparatus for detecting the presence of the labeling agent

comprising an excitation source illuminating a vessel with a photodetector directly within the illuminated area is also shown. The photodetector is insensitive to the spectrum of the excitation source.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 436/546.000
INCLS: 436/500.000; 436/547.000; 436/800.000
NCL NCLM: 436/546.000
NCLS: 436/500.000; 436/547.000; 436/800.000

L12 ANSWER 24 OF 37 USPATFULL
AN 87:58546 USPATFULL
TI Visualization polymers and their application to diagnostic medicine
IN Ward, David C., Guilford, CT, United States
Leary, Jeffry J., East Haven, CT, United States
Brigati, David J., Hershey, PA, United States
PA Yale University, New Haven, CT, United States (U.S. corporation)
PI US 4687732 870818
AI US 83-503298 830610 (6)
DT Utility
EXNAM Primary Examiner: Marantz, Sidney
LREP Haley, Jr., James F.
CLMN Number of Claims: 45
ECL Exemplary Claim: 23
DRWN 7 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 1973
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for detecting a minute quantity of an inorganic or organic target molecule by combining it with a composition of a detecting agent for the target molecule which carries, by direct or indirect means, a visualization polymer. The visualization polymer is composed of multiple units of a visualization monomer which are covalently linked together directly or indirectly covalently linked together by coupling agents which bond to chemical groups of the monomer. The monomer may be an enzyme, a tagged polypeptide, a tagged polyol, a tagged polyolefin or a tagged carbohydrate. The detecting agent may be an antibody, an enzyme, a lectin, strand of a DNA receptor protein, avidin, streptavidin and the like. The visualization polymer produces a high degree of amplification for the detection of the target molecule.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/006.000
INCLS: 435/007.000; 435/014.000; 435/021.000; 435/025.000; 435/028.000; 435/188.000; 435/810.000; 436/501.000; 436/504.000; 436/537.000; 436/545.000; 436/546.000;

436/800.000; 436/801.000; 436/804.000; 436/808.000;
436/827.000
NCL NCLM: 435/006.000
NCLS: 435/007.400; 435/007.500; 435/007.720; 435/007.900;
435/014.000; 435/021.000; 435/025.000; 435/028.000;
435/188.000; 435/810.000; 435/968.000; 435/975.000;
436/501.000; 436/504.000; 436/537.000; 436/545.000;
436/546.000; 436/800.000; 436/801.000; 436/804.000;
436/808.000; 436/827.000; 536/024.300; 536/025.320

L12 ANSWER 25 OF 37 USPATFULL
AN 86:71521 USPATFULL
TI Homogeneous specific binding assay method
IN Bolguslaski, Robert C., Elkhart, IN, United States
Carrico, Robert J., Bremen, IN, United States
Christner, James E., Ann Arbor, MI, United States
PA Miles Laboratories, Inc., Elkhart, IN, United States (U.S. corporation)
PI US 4629688 861216
AI US 78-894836 780410 (5)
RLI Continuation of Ser. No. US 76-667996, filed on 18 Mar 1976, now abandoned which is a continuation-in-part of Ser. No. US 75-572008, filed on 28 Apr 1975, now abandoned
DT Utility
EXNAM Primary Examiner: Naff, David M.
LREP Klawitter, Andrew L.
CLMN Number of Claims: 42
ECL Exemplary Claim: 32
DRWN 12 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 2422
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A test composition, device, and method for their use in a homogeneous specific binding assay which employs a substance having reactant activity, i.e., a reactant, as a labeling substance in the detection of a **ligand** in a liquid medium. The test composition and device comprise a conjugate formed of a specific binding substance coupled to the reactant. The reactant advantageously is an enzymatic reactant such as an enzyme substrate or coenzyme. The activity of the conjugated reactant as a constituent of a predetermined reaction is affected by reaction between the specific binding substance in the conjugate and a specific binding counterpart thereto. The presence of a **ligand** in a liquid medium may be determined using competitive or displacement binding or sequential saturation techniques wherein the specific binding substance in the conjugate is the **ligand** or a specific binding analog thereof, or using a direct binding technique wherein the specific binding substance is a specific binding partner of the **ligand**. The effect of the specific binding reaction on the activity of the

conjugated reactant is related to the presence or amount of the **ligand** in the liquid medium tested.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/007.000
INCLS: 435/174.000; 436/537.000; 436/544.000; 436/546.000
NCL NCLM: 435/007.700
NCLS: 435/007.500; 435/007.710; 435/007.720; 435/174.000; 435/966.000; 436/537.000; 436/544.000; 436/546.000

L12 ANSWER 26 OF 37 USPATFULL
AN 85:63938 USPATFULL
TI **Ligand** analog-irreversible enzyme inhibitor conjugates
IN Voss, Houston F., Libertyville, IL, United States
Plattner, Jacob, Libertyville, IL, United States
Herrin, Thomas R., Waukegan, IL, United States
PA Abbott Laboratories, North Chicago, IL, United States (U.S. corporation)
PI US 4550163 851029
AI US 81-228414 810126 (6)
RLI Division of Ser. No. US 79-9007, filed on 5 Feb 1979, now patented, Pat. No. US 4273866
DT Utility
EXNAM Primary Examiner: Sutto, Anton H.
LREP Katz, Martin L.; O'Brien, Margaret M.
CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1167
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention encompasses a method for determining **ligands** in test samples comprising intermixing with the test sample a **ligand** analog-irreversible enzyme inhibitor conjugate and a binding protein bindable to the **ligand** and the **ligand** analog-irreversible enzyme inhibitor conjugate and wherein the amount of **ligand** analog-irreversible enzyme inhibitor conjugate bound by the binding protein is related to the amount of **ligand** in the test sample, said binding protein inactivating the irreversible enzyme inhibitor when bound to the **ligand** analog portion of the conjugate; intermixing an enzyme which is irreversibly inhibited by the **ligand** analog-irreversible enzyme inhibitor conjugate unbound by the binding protein; and intermixing substrate to the enzyme and monitoring the enzyme substrate reaction.

The invention also includes **ligand** analog-irreversible enzyme inhibitor conjugates useful as reagents in practicing the method. Methods and reagents of the present are particularly

useful in determining drugs, hormones, and the like in biological fluids.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 544/244.000
INCLS: 260/944.000; 260/397.400; 260/397.500; 260/397.200; 536/013.600; 536/025.000; 548/413.000
NCL NCLM: 544/244.000
NCLS: 536/013.600; 536/026.400; 536/026.410; 536/026.440; 540/004.000; 540/005.000; 540/102.000; 548/413.000; 552/505.000; 552/506.000; 987/159.000

L12 ANSWER 27 OF 37 USPATFULL
AN 85:3261 USPATFULL
TI Soluble immunoassay reagent comprising lectin covalently bonded to reactive component
IN Chu, Albert E., San Mateo, CA, United States
PA E-Y Laboratories, San Mateo, CA, United States (U.S. corporation)
PI US 4493793 850115
AI US 81-292739 810814 (6)
RLI Division of Ser. No. US 78-972921, filed on 26 Dec 1978, now patented, Pat. No. US 4371515
DT Utility
EXNAM Primary Examiner: Fagelson, Anna P.
LREP Flehr, Hohbach, Test, Albritton & Herbert
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 573
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A lectin is covalently bonded to an immunological conjugate such as an antibody-antigen or its equivalent. Then, the lectin-conjugate is isolated from the reaction product mixture by one of a number of alternative techniques involving one or more of the following types of reaction; (1) reversible reaction of the lectin with an insolubilized sugar to isolate lectin from the remainder of the mixture, (2) reaction of one immunological component (e.g., antibody) bonded to the lectin with an insolubilized corresponding component (e.g., antigen) to separate the antibody components from the remainder of the reaction mixture, and (3) filtration of the reaction components to separate on the basis of product molecular weight, size and/or shape of the components.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 260/112.000R
INCLS: 260/112.500R; 424/011.000; 424/085.000; 424/088.000; 424/177.000; 424/195.000; 436/500.000; 436/501.000; 436/503.000; 436/528.000; 436/529.000; 436/827.000;

435/007.000
NCL NCLM: 530/303.000
NCLS: 424/085.100; 435/005.000; 435/006.000; 435/007.230; 435/007.800; 436/500.000; 436/501.000; 436/503.000; 436/528.000; 436/529.000; 436/543.000; 436/547.000; 436/827.000; 530/345.000; 530/358.000; 530/359.000; 530/362.000; 530/363.000; 530/380.000; 530/386.000; 530/391.100; 530/392.000; 530/395.000; 530/396.000; 530/397.000; 530/398.000; 530/399.000; 530/400.000; 530/403.000; 530/405.000; 530/406.000; 530/806.000; 530/807.000; 530/862.000; 530/863.000

L12 ANSWER 28 OF 37 USPATFULL
AN 84:58311 USPATFULL
TI Method and apparatus for performing assays
IN Miles, Laughton E., Stanford, CA, United States
Rogers, Jr., Arthur H., Los Altos, CA, United States
Rogers, Charles H., Duxbury, MA, United States
PA Medical & Scientific, Inc., Rockland, MA, United States (U.S. corporation)
PI US 4477578 841016
AI US 82-354848 820304 (6)
DT Utility
EXNAM Primary Examiner: Marcus, Michael S.
LREP Townsend & Townsend
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 1192
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Method and apparatus are provided for carrying out multiple simultaneous transfers of fluid. The method and apparatus are particularly directed toward immunoassays wherein immunologically active compounds, such as antigens and haptens, are detected through their associated antibodies. The device relies on the ability to transfer fluids, such as biological samples and reagents, between a reservoir and an associated receptacle. By providing a receptacle having a port at its lower end and which is otherwise hermetically sealed, such fluid transfer can be effected by immersing the port beneath the surface of the fluid in the reservoir and manipulating the pressure on the remaining surface area outside the port. The transfer of biological fluids at positive pressure provides enhanced fluids flow characteristics, particularly reduction or elimination of the tendency of these fluids to froth or bubble. Moreover, since the fluids can easily be manipulated, they can be agitated to speed up the reaction and reduce the overall reaction time and can be transferred from the reaction zone to allow interim measurements of the extent of reaction to provide for a rate mode assay. The method and

apparatus also find use in preparing solid phase reagents for use in assay systems, as well as a highly accurate pipetting system in analytic applications not limited to immunoassays.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 436/518.000
INCLS: 073/864.010; 141/001.000; 141/005.000; 141/051.000; 118/050.000; 422/064.000; 422/068.000; 422/100.000; 422/102.000; 422/061.000; 422/067.000; 422/071.000; 436/500.000; 436/501.000; 436/513.000; 436/527.000; 436/548.000; 436/545.000; 436/542.000; 436/807.000; 436/808.000; 436/810.000; 436/847.000; 436/057.000; 436/178.000; 436/180.000; 436/820.000
NCL NCLM: 436/518.000
NCLS: 073/864.010; 118/050.000; 141/001.000; 141/005.000; 141/051.000; 422/064.000; 422/100.000; 422/102.000; 436/047.000; 436/500.000; 436/501.000; 436/513.000; 436/527.000; 436/542.000; 436/545.000; 436/548.000; 436/807.000; 436/808.000; 436/810.000; 436/820.000

L12 ANSWER 29 OF 37 USPATFULL
AN 84:25940 USPATFULL
TI Homogeneous specific binding assay with carrier matrix incorporating specific binding partner
IN Rupchock, Patricia A., Elkhart, IN, United States
Tyhach, Richard J., Elkhart, IN, United States
PA Miles Laboratories, Inc., Elkhart, IN, United States (U.S. corporation)
PI US 4447526 840508
AI US 81-255521 810420 (6)
DT Utility
EXNAM Primary Examiner: Marantz, Sidney
LREP Gorman, Jr., Edward H.
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 756
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for determining the presence of a **ligand** in, or the **ligand** binding capacity of a liquid test sample which includes the steps of (a) adding to the sample a conjugate of the **ligand** and a label, (b) contacting the sample with a test device containing reagents which in conjunction with the conjugate and **ligand**, are capable of producing a detectable response, and (c) measuring the response.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/007.000
INCLS: 422/056.000; 435/805.000; 436/528.000; 436/530.000;

436/535.000; 436/537.000; 436/810.000
NCL NCLM: 435/007.700
NCLS: 422/056.000; 435/007.720; 435/007.920; 435/805.000; 435/971.000; 436/528.000; 436/530.000; 436/535.000; 436/537.000; 436/810.000

L12 ANSWER 30 OF 37 USPATFULL
AN 84:10208 USPATFULL
TI Diamine acid fluorescent chelates
IN Wieder, Irwin, Los Altos, CA, United States
Wollenberg, Robert H., Los Altos, CA, United States
PA Analytical Radiation Corporation, Los Altos, CA, United States (U.S. corporation)
PI US 4432907 840221
AI US 81-260574 810505 (6)
RLI Division of Ser. No. US 79-73728, filed on 10 Sep 1979, now patented, Pat. No. US 4352751
DT Utility
EXNAM Primary Examiner: Gron, Teddy S.
LREP Burns, Doane, Swecker & Mathis
CLMN Number of Claims: 30
ECL Exemplary Claim: 1,17,30
DRWN No Drawings
LN.CNT 892
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Species-linked diamine triacetic acids of the formula ##STR1## wherein T is an organic species containing at least one amine, hydroxyl, or thio functional group, L is the residue of at least one of those functional groups and R is a two or more atom long covalent bridge, are disclosed. Methods for their preparation, for the preparation of metal chelates from them and for the use of the chelates are also disclosed. In a preferred embodiment, the metal ions employed in the formation of the chelates are rare earth metal ions capable of forming fluorescent chelates which can in turn be employed in fluoroassay techniques.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 260/429.200
INCLS: 424/007.100; 252/301.160; 252/301.170; 252/301.180; 260/429.000J; 260/429.100; 260/112.000R; 260/112.500R; 260/113.000; 260/112.000T; 260/112.700; 260/124.000R; 560/169.000; 562/448.000; 562/507.000; 562/565.000; 562/566.000; 435/004.000; 435/007.000; 436/500.000; 436/501.000; 436/503.000; 436/543.000; 436/546.000; 436/513.000; 436/056.000; 436/172.000; 436/547.000; 436/537.000
NCL NCLM: 534/016.000
NCLS: 252/301.160; 252/301.170; 252/301.180; 435/004.000; 435/964.000; 435/968.000; 436/056.000; 436/172.000;

436/500.000; 436/501.000; 436/503.000; 436/513.000;
436/537.000; 436/543.000; 436/546.000; 436/547.000;
530/802.000; 560/169.000; 562/448.000; 562/507.000;
562/565.000; 562/566.000

L12 ANSWER 31 OF 37 USPATFULL
AN 83:18177 USPATFULL
TI Homogeneous chemiluminescent specific binding assay
IN Boguslaski, Robert C., Elkhart, IN, United States
Carrico, Robert J., Bremen, IN, United States
PA Miles Laboratories, Inc., Elkhart, IN, United States (U.S. corporation)
PI US 4383031 830510
AI US 79-50620 790621 (6)
RLI Division of Ser. No. US 78-894836, filed on 10 Apr 1978, now Defensive Publication No. which is a continuation of Ser. No. US 76-667996, filed on 18 Mar 1976, now abandoned which is a continuation-in-part of Ser. No. US 75-572008, filed on 28 Apr 1975, now abandoned
DT Utility
EXNAM Primary Examiner: Marantz, Sidney
LREP Klawitter, Andrew L.
CLMN Number of Claims: 46
ECL Exemplary Claim: 1,37
DRWN 12 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 2460
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A homogeneous specific binding assay which employs a substance having reactant activity, i.e., a reactant, in a chemiluminescent reaction as a labeling substance in the detection of a **ligand** in a liquid medium. The assay employs a conjugate formed of a specific binding substance coupled to the chemiluminescent reactant. The activity of the conjugated reactant as a constituent of the chemiluminescent reaction is affected by reaction between the specific binding substance in the conjugate and a specific binding counterpart thereto. The presence of a **ligand** in a liquid medium may be determined using competitive or displacement binding or sequential saturation techniques wherein the specific binding substance in the conjugate is the **ligand** or a specific binding analog thereof, or using a direct binding technique wherein the specific binding substance is a specific binding partner of the **ligand**. The effect of the specific binding reaction on the chemiluminescent activity of the conjugated reactant is related to the presence or amount of the **ligand** in the liquid medium tested.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/007.000

INCLS: 422/061.000; 436/536.000; 436/805.000; 436/808.000; 436/817.000
NCL NCLM: 435/007.720
NCLS: 422/061.000; 435/007.500; 435/007.700; 435/007.910; 435/007.930; 435/968.000; 435/971.000; 436/536.000; 436/805.000; 436/808.000; 436/817.000

L12 ANSWER 32 OF 37 USPATFULL
AN 83:5360 USPATFULL
TI Method for forming an isolated lectin-immunological conjugate
IN Chu, Albert E., San Mateo, CA, United States
PA E-Y Laboratories, Inc., San Mateo, CA, United States (U.S. corporation)
PI US 4371515 830201
AI US 78-972921 781226 (5)
DT Utility
EXNAM Primary Examiner: Fagelson, Anna P.
LREP Flehr, Hohbach, Test, Albritton & Herbert
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 682
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A lectin is covalently bonded to an immunological conjugate such as an antibody-antigen or its equivalent. Then, the lectin-conjugate is isolated from the reaction product mixture by one of a number of alternative techniques involving one or more of the following types of reaction; (1) reversible reaction of the lectin with an insolubilized sugar to isolate lectin from the remainder of the mixture, (2) reaction of one immunological component (e.g., antibody) bonded to the lectin with an insolubilized corresponding component (e.g., antigen) to separate the antibody components from the remainder of the reaction mixture, and (3) filtration of the reaction components to separate on the basis of product molecular weight, size and/or shape of the components.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 436/544.000
INCLS: 260/112.000R; 424/001.500; 424/085.000; 424/088.000; 424/177.000; 424/180.000; 435/007.000; 436/827.000; 436/548.000
NCL NCLM: 436/544.000
NCLS: 435/007.800; 435/961.000; 436/543.000; 436/547.000; 436/548.000; 436/827.000; 514/001.000; 530/341.000; 530/391.100; 530/396.000; 530/405.000; 530/413.000

L12 ANSWER 33 OF 37 USPATFULL
AN 82:48358 USPATFULL

TI Species-linked diamine triacetic acids and their chelates
IN Wieder, Irwin, Los Altos, CA, United States
Wollenberg, Robert H., Los Altos, CA, United States
PA Analytical Radiation Corporation, Los Altos, CA, United States
(U.S. corporation)
PI US 4352751 821005
AI US 79-73728 790910 (6)
DT Utility
EXNAM Primary Examiner: Gron, Teddy S.
LREP Burns, Doane, Swecker & Mathis
CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 867
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Species-linked diamine triacetic acids of the formula ##STR1## wherein T is an organic species containing at least one amine, hydroxyl, or thiol functional group, L is the residue of at least one of those functional groups and R is a two or more atom long covalent bridge, are disclosed. Methods for their preparation, for the preparation of metal chelates from them and for the use of the chelates are also disclosed. In a preferred embodiment, the metal ions employed in the formation of the chelates are rare earth metal ions capable of forming fluorescent chelates which can in turn be employed in fluoroassay techniques.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 260/112.000R
INCLS: 560/169.000; 562/448.000; 562/507.000; 562/565.000; 562/566.000; 023/230.000B; 252/301.160; 252/301.170; 252/301.180; 260/112.000T; 260/112.500R; 260/112.700; 260/113.000; 260/124.000R; 260/397.200; 260/429.000J; 260/429.100; 260/429.200; 260/455.000R; 424/001.000; 424/001.500; 424/007.000; 424/008.000; 424/012.000; 435/004.000; 435/007.000
NCL NCLM: 530/303.000
NCLS: 252/301.160; 252/301.170; 252/301.180; 435/004.000; 435/007.210; 435/007.320; 435/007.400; 435/188.000; 435/968.000; 436/071.000; 436/086.000; 436/500.000; 436/513.000; 436/532.000; 436/536.000; 436/546.000; 530/345.000; 530/391.500; 530/398.000; 530/399.000; 530/404.000; 530/405.000; 530/408.000; 530/409.000; 530/862.000; 530/868.000; 534/013.000; 534/016.000; 544/064.000; 552/544.000; 556/001.000; 556/044.000; 556/050.000; 556/056.000; 556/063.000; 556/077.000; 556/107.000; 556/116.000; 556/134.000; 556/136.000; 556/137.000; 556/148.000; 556/175.000; 558/253.000; 560/169.000; 562/448.000; 562/507.000; 562/565.000; 562/566.000

L12 ANSWER 34 OF 37 USPATFULL
AN 81:50449 USPATFULL
TI Immunological determination using lectin
IN Chu, Albert E., San Mateo, CA, United States
PA E-Y Laboratories, Inc., San Mateo, CA, United States (U.S. corporation)
PI US 4289747 810915
AI US 78-972696 781226 (5)
DT Utility
EXNAM Primary Examiner: Padgett, Benjamin R.; Assistant Examiner: Nucker, Christine M.
LREP Flehr, Hohbach, Test, Albritton & Herbert
CLMN Number of Claims: 48
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1155
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for the determination of one or more components of an immunological conjugate, e.g., antigens, of a fluid sample in a competitive or sandwich technique in which the conjugate is labelled and separated from its reactive mixture by reversible attachment to a solid surface. In a preferred embodiment, the solid surface comprises insolubilized sugar which reversibly bonds to a lectin covalently bonded to one member of the conjugate. After separation of such solid surface from the remainder of the reaction mixture, the insolubilized sugar-lectin bond is broken by contact with a sugar solution which displaces the labelled lectin compound. The immunological components including label and lectin may be preincubated in a homogeneous solution prior to reversible attachment to the sugar solid surface. For a competitive system, a sample containing antigen is incubated with a known quantity of labelled antigen and lectin-bound antibody. In the sandwich technique, the sample antigen is incubated with lectin-bound antibody and further with labelled antibody and this reaction mixture is contacted with insolubilized sugar. Either the competitive or sandwich technique are adaptable to a sequential flowthrough system with sufficient residence time to eliminate the preliminary incubation steps.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/001.000
INCLS: 023/230.000B; 424/012.000; 435/007.000
NCL NCLM: 435/007.800
NCLS: 435/007.930; 435/007.940

L12 ANSWER 35 OF 37 USPATFULL
AN 81:33233 USPATFULL
TI **Ligand** analog-irreversible enzyme inhibitor conjugates

and methods for use
IN Voss, Houston F., Libertyville, IL, United States
Plattner, Jacob, Libertyville, IL, United States
Herrin, Thomas R., Waukegan, IL, United States
PA Abbott Laboratories, North Chicago, IL, United States (U.S. corporation)
PI US 4273866 810616
AI US 79-9007 790205 (6)
DT Utility
EXNAM Primary Examiner: Wiseman, Thomas G.
LREP McDonnell, John J.
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1154
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention encompasses a method for determining **ligands** in test samples comprising intermixing with the test sample a **ligand** analog-irreversible enzyme inhibitor conjugate and a binding protein bindable to the **ligand** and the **ligand** analog-irreversible enzyme inhibitor conjugate and wherein the amount of **ligand** analog-irreversible enzyme inhibitor conjugate bound by the binding protein is related to the amount of **ligand** in the test sample, said binding protein inactivating the irreversible enzyme inhibitor when bound to the **ligand** analog portion of the conjugate; intermixing an enzyme which is irreversibly inhibited by the **ligand** analog-irreversible enzyme inhibitor conjugate unbound by the binding protein; and intermixing substrate to the enzyme and monitoring the enzyme substrate reaction.

The invention also includes **ligand** analog-irreversible enzyme inhibitor conjugates useful as reagents in practicing the method. Methods and reagents of the present are particularly useful in determining drugs, hormones, and the like in biological fluids.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/007.000
INCLS: 435/020.000; 435/184.000; 435/810.000; 424/012.000; 023/230.000B
NCL NCLM: 435/007.710
NCLS: 435/007.800; 435/020.000; 435/184.000; 435/810.000; 435/962.000; 436/500.000; 436/536.000; 436/825.000; 544/244.000; 987/159.000

L12 ANSWER 36 OF 37 USPATFULL
AN 80:54931 USPATFULL

TI Methods for performing chemical assays using fluorescence and photon counting
IN Dowben, Robert M., Dallas, TX, United States
Bunting, James R., Boston, MA, United States
PA Diagnostic Reagents, Inc., Dallas, TX, United States (U.S. corporation)
PI US 4231750 801104
AI US 77-860168 771213 (5)
RLI Continuation-in-part of Ser. No. US 75-634797, filed on 24 Nov 1975, now abandoned
DT Utility
EXNAM Primary Examiner: Marantz, Sidney
LREP Richards, Harris & Medlock
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1014
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Improved methods for determining very low concentrations of substances present in fluid samples are provided by employing light emitting tracer compounds and (1) counting the photons emitted therefrom while discriminating against noise, nonspecific light, and quenching effects of the sample, or (2) counting the photons emitted therefrom over a predetermined integrated light flux, or a combination of (1) and (2). Further, novel fluorescently labeled low molecular weight antigens are provided which can be employed in competitive binding techniques in which the above described photon counting methods are useful. A homogeneous competitive binding assay, employing photon emitting tracer materials, which eliminates the need for separating bound from unbound materials is also provided. Finally, a modified enzyme amplification technique is set forth employing enzymes active in the bound phase to provide assay techniques useful for extremely low concentration assays.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 023/230.000B
INCLS: 023/915.000; 424/008.000; 424/012.000; 435/004.000; 250/459.000
NCL NCLM: 436/546.000
NCLS: 250/302.000; 250/459.100; 435/004.000; 436/518.000; 436/527.000; 436/531.000; 436/533.000; 436/547.000

L12 ANSWER 37 OF 37 USPATFULL
AN 78:3440 USPATFULL
TI Assay for bilirubin
IN Wu, Tai-Wing, Rochester, NY, United States
PA Eastman Kodak Company, Rochester, NY, United States (U.S. corporation)

PI US 4069016 780117
AI US 77-759530 770114 (5)
DT Utility
EXNAM Primary Examiner: Reese, Robert M.
LREP Hilst, Ronald P.
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 1772
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for the determination of bilirubin in liquid samples, particularly biological liquid samples. An assay method, as well as an analytical element, is disclosed. In accord with the assay method there are contacted together a liquid sample containing bilirubin as analyte and an interactive composition containing a bilirubin-active complex, the complex comprising a diffusible, bilirubin-displaceable, detectable **ligand** bound to a carrier which can also bind bilirubin. As a result of a competitive binding-displacement interaction between bilirubin and the complex, bilirubin binds to the carrier and displaces detectable **ligand** which can be selectively detected and used to determine the presence or amount of bilirubin. Appropriate carriers and detectable **ligands** can be chosen on the basis of their first order binding constants.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 023/230.000B
INCLS: 023/253.000TP
NCL NCLM: 436/097.000
NCLS: 436/172.000

=> d his l13-; d 1-13 bib abs

(FILE 'BIOSIS, MEDLINE, EMBASE, LIFESCI, BIOTECHDS, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, PROMT, CIN, CBNB, CEN, DRUGU, DRUGNL, DRUGB' ENTERED AT 11:15:20 ON 23 DEC 1998)
L13 29 S L11
L14 13 DUP REM L13 (16 DUPLICATES REMOVED)

L14 ANSWER 1 OF 13 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 1
AN 1994:31299 BIOSIS
DN PREV199497044299
TI A naturally occurring furan fatty acid enhances drug inhibition of **thyroxine** binding in serum.
AU Lim, Chen-Fee; Stockigt, Jan R. (1); Curtis, Andrea J.; Wynne, Kenneth N.; Barlow, John W.; Topliss, Duncan J.
CS (1) Ewen Downie Metabolic Unit, Alfred Hosp., Commercial Rd., Melbourne, VIC 3181 Australia
SO Metabolism Clinical and Experimental, (1993) Vol. 42, No. 11, pp.

1468-1474.
ISSN: 0026-0495.
DT Article
LA English
AB We studied the **thyroxine** (T-4)-displacing effects of a naturally occurring, highly albumin-bound furanoid acid that accumulates in serum in renal failure to concentrations in excess of 0.2 mmol/L. This substance, 3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid (CMPF), has been shown to displace acidic drugs from albumin binding. The effects of CMPF on **ligand** binding were assessed in the following systems: (1) T-4 binding to T-4-binding globulin (TBG) and transthyretin (TTR), (2) T-4 binding in undiluted serum, (3) T-4-displacing potency of fenclofenac, furosemide, diflunisal, and aspirin in undiluted serum, (4) serum binding of (14C)-drug preparations, and (5) serum binding of (14C)-**oleic** acid. CMPF had a minor direct effect on T-4 binding to TBG comparable in relative affinity to that of aspirin, ie, almost 7 orders of magnitude less than T-4 itself. CMPF alone at a concentration of 0.3 mmol/L, which produced only a 10% to 14% increase in free T-4 augmented the T-4-displacing effects of high therapeutic concentrations of the various drugs in undiluted serum as follows: furosemide by 180%, fenclofenac by 160%, diflunisal by 130%, and aspirin by 40%. In the presence of fenclofenac, increments of CMPF from 0.075 to 0.3 mmol/L progressively augmented the T-4-displacing effect of this drug, associated with a progressive increase in its calculated free concentration. CMPF also inhibited the binding of (14C)-**oleic** acid, suggesting that in some situations CMPF could also indirectly influence thyroid hormone binding by increasing the unbound concentration of nonesterified fatty acids (NEFA), as previously described. CMPF at a concentration of 1 mmol/L did not inhibit charcoal or talc uptake of **triiodothyronine** (T-3) or T-4. These findings indicate that CMPF can inhibit specific T-4 binding in serum by increasing the free concentrations of direct competitors. Such "cascade effects" on thyroid hormone binding could influence both the circulating concentrations and tissue delivery of thyroid hormones in renal failure and critical illness.

L14 ANSWER 2 OF 13 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 2
AN 1992:26489 BIOSIS
DN BA93:15764
TI INTERACTIONS BETWEEN **OLEIC** ACID AND DRUG COMPETITORS INFLUENCE SPECIFIC BINDING OF **THYROXINE** IN SERUM.
AU LIM C-F; CURTIS A J; BARLOW J W; TOPLISS D J; STOCKIGT J R
CS EWEN DOWNIE METABOLIC UNIT, ALFRED HOSP., COMMERCIAL ROAD, MELBOURNE, VICTORIA 3181, AUST.
SO J CLIN ENDOCRINOL METAB, (1991) 73 (5), 1106-1110.
CODEN: JCEMAZ. ISSN: 0021-972X.
FS BA; OLD

LA English

AB Long chain nonesterified fatty acids and various drugs may share albumin-binding sites in common. We questioned whether serum binding of T4 could be indirectly influenced by displacement of drug competitors from these sites by nonesterified fatty acids. The influence of **oleic** acid on drug-induced inhibition of [125I]T4 binding was measured by equilibrium dialysis, using undiluted serum in order to avoid dilution-related artifacts. **Oleic** acid (1 mmol/L) alone did not inhibit serum protein binding of T4, but this concentration augmented the inhibitory effects on T4 binding of diflunisal, mefenamic acid, meclofenamic acid, and aspirin. This effect increased with increasing concentrations of mefenamic acid, meclofenamic acid, and furosemide. The T4-displacing effect of fenclofenac was not augmented by **oleic** acid. The mechanism of these interactions was studied by examining 1) **oleic** acid effects on drug binding, and 2) drug effects on **oleic** acid binding in undiluted serum. Increments in added **oleic** acid (0.5-2.0 mmol/L) progressively increased the mean unbound fractions of [14C]aspirin, [14C]diflunisal, and [14C]furosemide, but did not displace [14C]fenclofenac. At the relevant total and free drug concentrations, the inhibitory efect of **oleic** acid on drug binding and its influence on drug-induced displacement of T4 were concordant in the order: meclofenamic acid > aspiring > mefenamic acid > diflunisal > furosemide > fenclofenac. In contrast, drug-induced increases in the unbound fraction of [14C]**oleic** acid did not correlate with augmentation of T4 displacement. We conclude that synergistic effects of **oleic** acid and drugs on T4 binding result from drug displacement by **oleic** acid, rather than the reverse effect. Hence, substances that increases the unbound concentration of a competitor by displacing it from albumin can increase its T4-displacing potency. Interactions between various **ligands** may exert a greater hormone-displacing effect than the sum of each alone.

L14 ANSWER 3 OF 13 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 3

AN 1989:316358 BIOSIS

DN BA88:30088

TI DRUG COMPETITION FOR **THYROXINE** BINDING TO TRANSTHYRETIN PREALBUMIN COMPARISON WITH EFFECTS ON **THYROXINE**-BINDING GLOBULIN.

AU MUNRO S L; LIM C-F; HALL J G; BARLOW J W; CRAIK D J; TOPLISS D J; STOCKIGT J R

CS EWEN DOWNIE METABOLIC UNIT, ALFRED HOSP., COMMERCIAL RD., MELBOURNE, VICTORIA 3181, AUST.

SO J CLIN ENDOCRINOL METAB, (1989) 68 (6), 1141-1147. CODEN: JCEMAZ. ISSN: 0021-972X.

FS BA; OLD

LA English

AB We examined the effect of 26 drugs on T4 binding to transthyretin (TTR; prealbumin) and T4-binding globulin (TBG) by determining their ability to inhibit [125I]T4 binding to TTR isolated from normal human plasma and to serum diluted 1:10,000, respectively. The hierarchies for drug inhibition of T4 binding differed greatly for these two proteins. Relative to T4, the drugs were much more potent inhibitors of [125I]T4 binding to TTR than to TBG. Compounds of the anthranilic acid class, such as flufenamic, meclofenamic, and mefenamic acids, interacted particularly strongly with TTR. Flufenamic acid was more potent than T4 itself in inhibiting [125I]T4 binding [175 .+-. 17% (.+-. SD); cf. T4; in = 3; P < 0.001], while mefenamic acid, diflunisal, and meclofenamic acid were 20%-26% as potent as T4 in their interaction with TTR. The reactivity of diclofenac, fenclofenac, indomethacin, sulindac, and the diuretic ethacrynic acid was 0.8-2.1% relative to that of T4. In contrast, furosemide, the drug most highly reactive with TBG, was only 0.11 .+-. 0.03% (n = 7) as potent as T4, followed by meclofenamic acid > mefenamic acid > feclofenac > flufenamic acid > diflunisal > milrinone. Aspirin and **sodium salicylate** were, respectively, 0.05% and 0.20% as active as unlabeled T4 as inhibitors of [125I]T4 binding to TTR, but these compounds had only 3-4 .times. 10-6% of the activity of T4 for TBG binding. Diphenylhydantoin had no detectable effect on T4 binding to TTR and was 2.9 .times. 10-4% as reactive as T4 with TBG. Aminodarone did not interact with either binding site. Drug interactions with TTR may be important when this protein becomes a major circulating T4-binding protein, as in patients with complete or partial TBG deficiency, or when serum T4 is markedly elevated. Such interactions may also be important where TTR is the dominant tissue T4-binding protein, as in the choroid plexus. In addition, the drug competitors described here may be useful as probes to further define the structural basis for specific **ligand** interactions with different classes of T4-binding sites.

L14 ANSWER 4 OF 13 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 4
AN 1989:158910 BIOSIS
DN BA87:81011
TI UPTAKE OF 3 5 3' **TRIIODOTHYRONINE** BY CULTURED RAT HEPATOMA CELLS IS INHIBITABLE BY NONBILE ACID CHOLEPHILS DIPHENYLHYDANTOIN AND NONSTEROIDAL ANTIINFLAMMATORY DRUGS.
AU TOPLISS D J; KOLLINIATIS E; BARLOW J W; LIM C-F; STOCKIGT J R
CS EWEN DOWNIE METABOLIC UNIT, ALFRED HOSP., COMMERCIAL ROAD, MELBOURNE, VICTORIA, AUSTRALIA 3181.
SO ENDOCRINOLOGY, (1989) 124 (2), 980-986.
CODEN: ENDOAO. ISSN: 0013-7227.
FS BA; OLD
LA English
AB Cellular uptake of T3 was examined using rat H4 hepatoma cells. Uptake of [125I]T3 (10-11 M) from serum-free medium was measured as

the cell-associated counts retained by washed cells (2 .times. 106 per well). Displaceable uptake was 84% of total uptake at 2 min (2.9% of total counts). T4, tetraiodothyroacetic acid, triiodothyroacetic acid, rT3, and D-T3 was 2-5% as effective as T3 in displacing uptake. Nonequilibrium kinetics indicated a half-maximal uptake at 680 nM T3 with approximately 7 million sites per cell. Displaceable uptake was time and temperature dependent and was 73% inhibited by 2 mM KCN and 52% by 10 mM bacitracin but not by 2 mM ouabain or 10 .mu.M cytochalasin B. Phloretin, 100 .mu.M, inhibited uptake by 66%. T3 uptake was directly related to the free T3 concentration over the range of albumin concentrations, 0-10 g/liter. The nonbile acid cholephil compounds, bromosulfophthalein, iopanoic acid, and indocyanine green (all 100 .mu.M) inhibited t3 uptake to 62%, 17%, and 5% of control, respectively. Taurocholate, methylaminoisobutyric acid, and **oleic** acid were noninhibitory. The half-inhibitory concentrations of reactive nonsteroidal antiinflammatory drugs were: meclofenamic acid (25 .mu.M), mefenamic acid (45 .mu.M), fenclofenac (69 .mu.M), flufenamic acid (100 .mu.M), and diclofenac (230 .mu.m). Aspirin, ibuprofen, oxyphenbutazone, and phenylbutazone (all 100 .mu.M) were noninhibitory. Diphenylhydantoin inhibited uptake to 50% at 75 .mu.M. These findings suggest that T3 uptke by cultured rat hepatocytes is by an energy-dependent, saturable, stereo-selective mechanism that is dependent on cell membrane proteins. This mechanism appears to be shared by a number of other **ligands**, including nonbile acid cholephils and several nonsteroidal antiinflammatory drugs of the anthranilic and phenylacetic acid classes, as well as diphenylhydantoin. The bile acid taurocholate, **oleic** acid, and a probe for type A amino acid uptake were inactive. The extent to which these effects may modify expression of thyroid hormone action remains to be established.

L14 ANSWER 5 OF 13 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 5
AN 1989:267236 BIOSIS
DN BA88:3318
TI BINDING ACTIVITIES OF **THYROXINE** BINDING GLOBULIN VERSUS **THYROXINE** BINDING PREALBUMIN IN RAT SERA DIFFERENTIAL MODULATION BY THYROID HORMONE **LIGANDS OLEIC** ACID AND PHARMACOLOGICAL DRUGS.
AU SAVU L; VRANCKX R; MAYA M; NUNEZ E A
CS U.224, INSERM, FAC. DE MED. XAVIER BICHAT, 16, RUE HENRI HUCHARD-75018 PARIS, FRANCE.
SO BIOCHEM BIOPHYS RES COMMUN, (1989) 159 (3), 919-926. CODEN: BBRCA9. ISSN: 0006-291X.
FS BA; OLD
LA English
AB We use gel equilibration and electrophoretic technique to compare the binding properties of throxine binding globulin and **thyroxine** binding prealbumin rat sera. The evidence

indicates that TBG bears the serum lowest capacity highest affinity sites for **thyroxine** (T4) and **triiodothyronine** (T3) (Ka1 .gtoreq. 109M-1) as well as weaker saturable T3 sites (Ka2 .apprx. 108M-1). TBPA bears for T4 only Ka2 .apprx. 108M-1 sites and for T3 only Ka .apprx. 106M-1 sites. Consistent wth these parameters are the specific responses of TBG and TBPA binding activities to varying serum concentrations of T4, T3, **oleic** acid, the drugs diphenylhydantoin or salicylate. The primary attack of these compounds is aimed at TBG. Small T4, oleate or DPH doses chase the TBG-bound T4 to TBPA, high doses of T4 or oleate but not of DPH inhibiting the T4 binding to both proteins. In the T3-serum interactions, all tested compounds displace the TBG-bound hormone without chasing it to TBPA. The high reactivity of TBG sites designated the protein as crucially involved in modulating the free vs bound serum levels of T4 and T3 against physiological or pathological variations of binding competitors.

L14 ANSWER 6 OF 13 WPIDS COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 87-102765 [15] WPIDS
CR 95-233436 [31]
DNN N87-077286 DNC C87-042675
TI Determining free **ligand** in biological fluid esp, thyroid hormone - without disturbing equilibrium with protein bound **ligand** by using analogue tracer, specific **ligand** binder and chemical inhibitor.
DC B04 J04 K08 S03
IN EL, SHAMI A S; SHAMI, A S E; SAIDEISHAM, A; SAID, EL SHAMI A
PA (DIAG-N) DIAGNOSTIC PROD CORP; (DIAG-N) DIAGNOSTIC PRODUCTS CORP
CYC 9
PI EP 218309 A 870415 (8715)* EN 27 pp
AU 8657521 A 870409 (8720)
JP 62083666 A 870417 (8721)
NO 8602278 A 870427 (8723)
FI 8603186 A 870405 (8727)
DK 8602196 A 870405 (8729)
ES 8707342 A 871001 (8744)
IL 79283 A 910730 (9133)
CA 1299984 C 920505 (9223)
DK 169365 B 941010 (9439)
FI 92878 B 940930 (9439)
EP 218309 B1 951115 (9550) EN 23 pp
DE 3650437 G 951221 (9605)
JP 07311200 A 951128 (9605) 19 pp
JP 08001436 B2 960110 (9606) 17 pp
JP 2575338 B2 970122 (9708) 19 pp
ADT EP 218309 A EP 86-300336 860117; JP 62083666 A JP 86-157772 860704; ES 8707342 A ES 86-555425 860528; CA 1299984 C CA 86-510762 860604; DK 169365 B DK 86-2196 860512; FI 92878 B FI 86-3186 860805; EP 218309 B1 EP 86-300336 860117; DE 3650437 G DE 86-3650437 860117, EP

86-300336 860117; JP 07311200 A Div ex JP 86-157772 860704, JP 95-10194 860704; JP 08001436 B2 JP 86-157772 860704; JP 2575338 B2 Div ex JP 86-157772 860704, JP 95-10194 860704

FDT DK 169365 B Previous Publ. DK 8602196; FI 92878 B Previous Publ. FI 8603186; DE 3650437 G Based on EP 218309; JP 08001436 B2 Based on JP 62083666; JP 2575338 B2 Previous Publ. JP 07311200

PRAI US 85-784857 851004

AN 87-102765 [15] WPIDS

CR 95-233436 [31]

AB EP 218309 A UPAB: 950818

Concn. of a free **ligand** (I) in a biological fluid is measured in presence of bound (I) and endogenous binding proteins comprises (a) incubating a sample of the fluid with a **ligand** analogue tracer that, owing to its chemical structure, does not bind to some of the binding proteins but binds to at least one of them; a specific (I) binder; and a specific chemical inhibitor reagent(s) inhibiting the binding of the tracer to the at least one binding protein; (b) sepng. the tracer bound to the specific binder from unbound tracer; and (c) determng. the concn. of free (I) in the fluid, esp. by comparing the bound fraction in the sample with the bound fraction of a given set of free (I) calibrators.

USE/ADVANTAGE - With the procedure the equilibrium between the free (I) and protein-bound (I) is not disturbed, and a more true measurement of free (I)is obtd. (I) is a hormone, steroid, drug, drug metabolite, polypeptide, protein, vitamin, antigen, toxin etc., and esp. a thyroid hormone, e.g. **thyroxine** or triidothyroxine, or sex hormone, e.g. testosterone.

0/20

Dwg.0/20

ABEQ EP 218309 B UPAB: 951215

A method for measuring the concentration of free **thyroxine** or **triiodothyronine ligand** in a biological fluid in the presence of bound **ligand** and endogenous binding proteins including albumin, without disturbing the equilibrium between free **ligand** and protein-bound **ligand**, which method comprises (a) incubating a sample of the biological fluid with (i) a **ligand** analog tracer which, due to its chemical structure, does not bind to some of the endogenous binding proteins but does bind to at least one other endogenous binding protein including albumin, (ii) a concentration of a specific **ligand** binder having an affinity constant and selectivity for the free **ligand** such that the equilibrium between free **ligand** and protein-bound **ligand** is not disturbed and (iii) 25 mg/ml **sodium salicylate** and 0.15 mg/ml **2,4-di-nitrophenol**;
(b) separating the **ligand** analog tracer bound to the specific **ligand** binder from unbound tracer; and (c) determining the concentration of free **ligand** in said biological fluid.

Searcher : Shears 308-4994

Dwg.0/20

L14 ANSWER 7 OF 13 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 87-18350 DRUGU P
TI Protein Binding Studies of 99mTc Labeled Myocardial Imaging Agents.
AU Zanelli G D; Cook N; Lahiri A
LO Harrow, United Kingdom
SO Clin.Sci. (72, Suppl. 16, 87P, 1987)
CODEN: CSCIAE ISSN: 0143-5221
AV Division of Radioisotopes, Northwick Park Hospital and Clinical Research Centre, Harrow, Middlesex, England.
LA English
DT Journal
FA AB; LA; CT; MPC
FS Literature
AN 87-18350 DRUGU P
AB A novel 99mTc-labeled imaging agent, the phosphine-isocyanide complex (DEPE)2(CNR)2, where R is t-butyl (DEPIC), produced excellent myocardial perfusion images in rats, rabbits, and dogs. In humans, DEPIC behaved as a blood pool labeling agent and allowed high quality radionuclide ventriculography to be performed. Species variations in plasma protein binding could have accounted for the differences, DEPIC could be removed from human prealbumin by **Na salicylate**. Protein binding appears to be the key factor in the design of new Tc-99m **ligands** as substitutes for T1-201 for myocardial perfusion agents and alternative methods should be designed for testing newer substances in pre-human studies. (congress abstract).
ABEX DEPIC produced excellent myocardial perfusion images in animals (rats, rabbits, dogs). Heart to lung ratio was 15:1, heart to liver uptake was 5:1 for the rabbit. However, in human volunteer studies no myocardial uptake was noted but DEPIC behaved as a blood pool labeling agent (half-life 4.2 hr), and high quality radionuclide ventriculography could be performed. DEPIC was further characterized by slab-gel electrophoresis, column chromotography and molecular sizing. In humans DEPIC was strongly bound to prealbumin while in rabbits it was weakly bound to a variety of larger proteins. This difference may be due to the fact that prealbumin is a tetramer in humans, but a dimer in rabbits. DEPIC could be removed from the human prealbumin by **Na salicylate**, which suggests that it may occupy the **thyroxine** binding sites. (NPH)

L14 ANSWER 8 OF 13 BIOSIS COPYRIGHT 1998 BIOSIS
AN 1986:464830 BIOSIS
DN BR31:111838
TI EXCESS **OLEIC**-ACID INCREASES THE FREE FRACTION OF VARIOUS DRUG INHIBITORS OF SERUM BINDING OF **THYROXINE**.
AU STOCKIGT J R; LIM C-F

CS EWEN DOWNIE METAB. UNIT, ALFRED HOSP., MELBOURNE, AUST.
SO MEETING OF THE DEUTSCHE GESELLSCHAFT FUER ENDOKRINOLOGIE (GERMAN SOCIETY OF ENDOCRINOLOGY), MUNICH, WEST GERMANY, MAR. 12-15, 1986. ACTA ENDOCRINOL SUPPL. (1986) 111 (274), 109.
CODEN: ACEDAB. ISSN: 0300-9750.
DT Conference
FS BR; OLD
LA English

L14 ANSWER 9 OF 13 DRUGU COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 86-37106 DRUGU P E
TI Excess **Oleic** Acid Increases the Free Fraction of Various Drug Inhibitors of Serum Binding of T4.
AU Stockigt J R; Lim C F
LO Melbourne, Australia
SO Acta Endocrinol. (111, Suppl. 274, 109, 1986) 2 Tab. 3 Ref.
CODEN: ACENA7 ISSN: 0001-5598
AV Ewen Downie Metabolic Unit, Alfred Hospital, Melbourne, Australia.
LA English
DT Journal
FA AB; LA; CT; MPC
FS Literature
AN 86-37106 DRUGU P E
AB The Authors tested the hypothesis that the FFA, **oleic** acid (OA) binding to plasma albumin can indirectly influence serum 125I-labeled T4 binding by increasing the free fraction of albumin bound drugs (furosemide, fenclofenac and aspirin) that can directly inhibit T4 binding to **thyroxine** binding globulin (TBG). The results demonstrated a potentially important interaction between OA and some direct competitors for T4 serum binding. By altering the albumin binding of a direct competitor, the albumin bound fraction of OA may indirectly influence the binding of iodothyonines. Thus, OA, the FFA which is the largest occupant of albumin sites, could act indirectly to inhibit binding of **ligands** to specific, high affinity, low capacity sites such as TBG. (congress).
ABEX Free fractions of furosemide, fenclofenac and aspirin were measured with 14C-drug preparations by equilibrium dialysis at 37 deg, using undiluted serum with added increments of OA (0.53-2.7 mM). Excess OA increased the free fraction of aspirin and furosemide, but not of fenclofenac. Addition of 1.8 mM OA to serum modified the inhibitory effect of 22 uM furosemide and 1,350 uM aspirin on 125I-T4 binding in undiluted serum. (E54/RSV)

L14 ANSWER 10 OF 13 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 6
AN 1985:357290 BIOSIS
DN BA80:27282
TI INTERACTION OF FUROSEMIDE WITH SERUM **THYROXINE**-BINDING SITES IN-VIVO AND IN-VITRO STUDIES AND COMPARISON WITH OTHER

INHIBITORS.

AU STOCKIGT J R; LIM C F; BARLOW J W; WYNNE K N; MOHR V S; TOPLISS D J; HAMBLIN P S; SABTO J

CS EWEN DOWNIE METABOLIC UNIT, ALFRED HOSPITAL, COMMERCIAL ROAD, MELBOURNE, VICTORIA 3181, AUSTRALIA.

SO J CLIN ENDOCRINOL METAB, (1985) 60 (5), 1025-1031.
CODEN: JCEMAZ. ISSN: 0021-972X.

FS BA; OLD

LA English

AB The diuretic furosemide inhibits serum protein binding of T4 [**thyroxine**] in equilibrium dialysis, dextran-charcoal and competitive **ligand** binding separation systems and displaces [125I]T4 from isolated preparations of T4-binding globulin (TBG), prealbumin and albumin. Equilibrium dialysis studies of undiluted normal serum showed that about 10 .mu.g/ml furosemide increased the free T4 and free T3 [**triiodothyronine**] fractions. Displacement occurred at lower drug concentrations in sera with subnormal albumin and TBG levels. Binding of [14C]furosemide to TBG was inhibited by unlabeled T4, suggesting that furosemide and T4 share a common binding site. A single oral dose of 500 mg furosemide given to 5 patients maintained on peritoneal dialysis increased the percentage of charcoal uptake of [125I]T4 (using serum diluted 1:10) from 4.1 .+-. 1.0 (.+-. SE) to 10.8 .+-. 4.3 ($P < 0.01$) after 2 h, while decreasing total T3 from 75 .+-. 5 to 56 .+-. 13 ng/dl ($P < 0.01$) and total T4 from 6.7 .+-. 0.9 to 4.8 .+-. 0.8 .mu.g/dl ($P < 0.01$) after 5 h. Various **ligands** inhibited [125I]T4 binding to serum proteins in the following relative molar relationship: T4, 1; furosemide, 1.5 .times. 103; fenclofenac, 2 .times. 104, mefenamic acid, 2.5 .times. 104; diphenylhydantoin, 4 .times. 104; ethacrynic acid, 106; heparin, 5 .times. 105; 2-hydroxybenzoylglycine, 106; and **sodium salicylate**, 1.5 .times. 106. Apparently, furosemide competes for T4-binding sites on TBG, prealbumin and albumin, so that a single high dose can acutely lower total T4 and T3 levels. The drug is much more potent on a molar basis than other drug inhibitors of T4 binding, but at normal therapeutic concentrations, furosemide is unlikely to decrease serum T4 or T3. High doses, diminished renal clearance, hypoalbuminemia and low TBG accentuate its T4- and T3-lowering effect. Hence, furosemide should be considered a possible cause of low thyroid hormone levels in patients with critical illness. The significance of this drug in reports of impaired hormone and drug binding in renal failure requires further assessment.

L14 ANSWER 11 OF 13 BIOSIS COPYRIGHT 1998 BIOSIS DUPLICATE 7

AN 1984:282162 BIOSIS

DN BA78:18642

TI A COMPETITIVE **LIGAND** BINDING ASSAY FOR MEASUREMENT OF THYROID HORMONE BINDING INHIBITOR IN SERUM AND TISSUES.

AU CHOPRA I J; HUANG T-S; HURD R E; BEREDO A; SOLOMON D H
CS DEPARTMENT OF MEDICINE, UCLA CENTER FOR THE HEALTH SCIENCES, LOS ANGELES, CALIFORNIA 90024.
SO J CLIN ENDOCRINOL METAB, (1984) 58 (4), 619-628.
CODEN: JCEMAZ. ISSN: 0021-972X.
FS BA; OLD
LA English
AB A competitive **ligand**-binding assay (CLBA) is described for measurement of an inhibitor(s) of serum binding of T4 [**thyroxine**] in ether extracts of serum and in homogenates and extracts of tissues. The CLBA is based on the effect of thyroid hormone binding inhibitor (THBI) on partition of a constant amount of radiolabeled **ligand** ([125I]T4) between fixed amounts of serum and an anti-T4 antibody. The method is convenient, rapid, sensitive, and reproducible. The coefficient of variation averaged 8.9% within an assay and 12.8% between assays. Several fatty acids, e.g., arachidonic acid, lauric acid, linolenic acid, and linoleic acid, had potent THBI activity in the CLBA; arachidonic acid was more potent than the other fatty acids. Since **oleic** acid cross-reacted substantially with T4-binding sites on anti-T4, its THBI activity was examined by an equilibrium dialysis method; it was about 77% as potent as arachidonic acid. Arachidic, myristic, palmitic, and stearic acids, cholesterol, various phospholipids and triglycerides (triolein and tripalmitin) had little or no THBI activity in the CLBA. THBI activity was detected in the sera of 50% (60% when serum T4 was low and 42% when it was normal) of 34 patients with nonthyroid illnesses (NTI) when studied by CLBA and in 59% (67% when serum T4 was low and 53% when it was normal) of patients when determined by the inhibitory ratio (normalized dialysis ratio/normalized binding ratio). THBI values obtained by the CLBA correlated significantly ($r = 0.58$; $P < 0.001$) with those obtained by the inhibitory ratio method. The dose-response curve of an ether extract of pooled sera of hospitalized patients was parallel to that of arachidonic acid in the CLBA. Among various rat tissues, the small intestine had the most THBI activity in both homogenates and ether extracts of homogenates. Ether (2 vol) extracted about 63% of the THBI activity in small intestine homogenate at pH 5.2. THBI activity was demonstrable in all particulate fractions (especially mitochondria and endoplasmic reticulum) of small intestine homogenate; cytosol contained little or no THBI activity. THBI activity changed little after treatment of small intestine homogenate with trypsin or protease inhibitors. THBI activity of small intestine and liver homogenate was enhanced by storage at room temperature, by repeated freezing and thawing, and by treatment of homogenate with phospholipases. CLBA is a convenient and sensitive system for detection of THBI. THBI activity in the sera of patients with nonthyroidal illness and in normal rat tissues is probably associated with a lipid, and certain fatty acids appear to be promising THBI candidates. THBI activity does not depend on

tissue protease(s), and the small intestine is a potent source of THBI.

L14 ANSWER 12 OF 13 DRUGB COPYRIGHT 1998 DERWENT INFORMATION LTD
AN 82-01526 DRUGB P
TI MOLECULAR ASPECTS OF **LIGAND** BINDING TO SERUM ALBUMIN.
AU KRAGH HANSEN U
LO AARHUS,DEN.
SO PHARMACOL.REV. (33, NO.1, 17-53, 1981)
LA English
DT Journal

L14 ANSWER 13 OF 13 MEDLINE
AN 75206986 MEDLINE
DN 75206986
TI Studies on Z-Fraction. I. Isolation and partial characterization of low molecular weight **ligand**-binding protein from rat hepatic cytosol.
AU Warner M; Neims A H
SO CANADIAN JOURNAL OF PHYSIOLOGY AND PHARMACOLOGY, (1975 Jun) 53 (3) 493-500.
Journal code: CJM. ISSN: 0008-4212.
CY Canada
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197512
AB The Z-fraction has been defined operationally as a **ligand** -binding (bilirubin **sulfobromophthalein**) portion of rat hepatic cytosol that elutes in the molecular weight region of 10(4) daltons after gel filtration. Polyacrylamide gel electrophoreses under different conditions, as well as binding stoichiometry, confirm the anticipated heterogeneity of the Z-fraction. Three factors have contributed to the subsequent resolution of the Z-fraction and partial characterization of that protein within the fraction with **ligand**-binding properties (Z-protein): (1) the use of hexachlorophene as **ligand**; (2) the inclusion of glycerol, 20%, during isolation to prevent aggregation and loss of binding-activity; and (3) the development of a charcoal binding assay. Upon ion exchange chromatography, the Z-fraction resolves into a group of distinct protein components and an unidentified material with a high 260/280 nm absorbancy ratio. The one protein component with binding capacity exhibits homogeneity on polyacrylamide gel electrophoresis (11% gel, Ann. N.Y. Acad. Sci. 121, 404-427, 1964; and 15% gel with SDS). With use of the charcoal method, apparent dissociation constants for the interaction between Z-protein and hexachlorophene, bilirubin and L-**thyroxine**, were found to be 20, 50, and 350 muM, respectively. The Scatchard plot generated upon extrapolation an n value of 1.0 with assumption

of a molecular weight for Z-protein of 10(4) daltons.

=> d his l15-; d 1-7 bib abs

(FILE 'CAPLUS, BIOSIS, MEDLINE, EMBASE, LIFESCI, BIOTECHDS, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, PROMT, CIN, CBNB, CEN, DRUGU, DRUGNL, DRUGB, USPATFULL' ENTERED AT 11:22:21 ON 23 DEC 1998) Author

L15 262 S (EL SHAMI A? OR ELSHAMI A? OR SHAMI A?)/AU
L16 17 S L15 AND L9
L17 7 DUP REM L16 (10 DUPLICATES REMOVED)

L17 ANSWER 1 OF 7 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 1
AN 1996:714156 CAPLUS
DN 126:26907
TI Validation of an immunoassay for canine thyroid-stimulating hormone and changes in serum concentration following induction of hypothyroidism in dogs
AU Williams, David A.; Scott-Moncrieff, Catharine; Bruner, Joseph; Sustarsic, Dennis; Panosian-Sahakian, Niver; Unver, Ercan; **Shami, A. Said El**
CS School Veterinary Medicine, Purdue University, West Lafayette, IN, 47907-1248, USA
SO J. Am. Vet. Med. Assoc. (1996), 209(10), 1730-1732
CODEN: JAVMA4; ISSN: 0003-1488
PB American Veterinary Medical Association
DT Journal
LA English
AB The objective of this study was to validate a new immunoradiometric assay for canine TSH (cTSH) and to document changes in serum cTSH concn. during induction of hypothyroidism in 6 healthy adult male dogs. Sensitivity, specificity, precision, and accuracy of the cTSH assay were evaluated in vitro. Hypothyroidism was induced in dogs by i.v. administration of Na131I soln. Subsequently, L-**thyroxine** was administered orally to normalize serum **thyroxine** concns. The cTSH assay appeared to be specific and was sufficiently sensitive to detect cTSH in the serum of these dogs prior to induction of hypothyroidism. There was a 35-fold increase in mean serum cTSH concn. following induction of hypothyroidism, and 35 days after initiation of thyroid replacement therapy, mean serum cTSH concn. was not significantly greater than mean baseline value. Thus, assay of serum cTSH is likely to prove helpful in the differential diagnosis of primary, secondary, and tertiary hypothyroidism in dogs, and in monitoring response to thyroid hormone replacement treatment.

L17 ANSWER 2 OF 7 BIOSIS COPYRIGHT 1998 BIOSIS

AN 1995:333335 BIOSIS
DN PREV199598347635
TI An automated chemiluminescent enzyme immunoassay for free T4 as an adjunct to a third generation TSH assay.
AU Witherspoon, L. R. (1); Lapeyrolerie, T. (1); Bodlaender, P.; Knadler, L.; **El Shami, A. S.**
CS (1) Ochsner Clin. and Alton Ochsner Med. Found., New Orleans, LA USA
SO Clinical Chemistry, (1995) Vol. 41, No. S6 PART 2, pp. S70. Meeting Info.: 47th Annual Meeting of the American Association for Clinical Chemistry, Inc. Anaheim, California, USA July 16-20, 1995 ISSN: 0009-9147.
DT Conference
LA English

L17 ANSWER 3 OF 7 BIOSIS COPYRIGHT 1998 BIOSIS
AN 1995:333332 BIOSIS
DN PREV199598347632
TI Evaluation of an immunoradiometric assay for thyroid stimulating hormone in neonatal blood spot samples.
AU Sustarsic, D.; Kameya, G.; Hall, G.; Bodlaender, P.; Levine, E.; **El Shami, A. S.**
CS Diagnostic Prod. Corp., Los Angeles, CA USA
SO Clinical Chemistry, (1995) Vol. 41, No. S6 PART 2, pp. S69-S70. Meeting Info.: 47th Annual Meeting of the American Association for Clinical Chemistry, Inc. Anaheim, California, USA July 16-20, 1995 ISSN: 0009-9147.
DT Conference
LA English

L17 ANSWER 4 OF 7 BIOSIS COPYRIGHT 1998 BIOSIS
AN 1995:333269 BIOSIS
DN PREV199598347569
TI Can the TBG saturation index (TGB-SI) substitute for the free T4 index (FT4I.
AU Durham, A. P.; Lei, J.-D.; Panosian-Sahakian, N.; Laroya, R.; **Shami, A. S. El**
CS Diagnostic Products Corp., Los Angeles, CA USA
SO Clinical Chemistry, (1995) Vol. 41, No. S6 PART 2, pp. S55-S56. Meeting Info.: 47th Annual Meeting of the American Association for Clinical Chemistry, Inc. Anaheim, California, USA July 16-20, 1995 ISSN: 0009-9147.
DT Conference
LA English

L17 ANSWER 5 OF 7 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 2
AN 1988:143567 CAPLUS
DN 108:143567
TI Chemically blocked analog assays for free thyronines. II. Use of equilibrium dialysis to optimize the displacement by chemical

blockers of T4 analog and T3 analog from albumin while avoiding displacement of T4 and T3 from **thyroxine**-binding globulin

AU Witherspoon, Lynn R.; **Shami, A. Said El**; Shuler, Stanton E.; Neely, Harold; Sonnemaker, Robert; Gilbert, Susan S.; Alyea, Kristin

CS Ochsner Clin., Alton Ochsner Med. Found., New Orleans, LA, 70121, USA

SO Clin. Chem. (Winston-Salem, N. C.) (1988), 34(1), 17-23
CODEN: CLCHAU; ISSN: 0009-9147

DT Journal

LA English

AB Chem. blockers used to displace thyronine analog from albumin in analog kits for assay of free **thyroxine** (FT4) or free **triiodothyronine** (FT3) may also displace **thyroxine** (T4) or **triiodothyronine** (T3) from **thyroxine** -binding globulin (TBG), resulting in an apparent TBG dependence of results of free hormone ests. Equil. dialysis and antibody binding were used to assess the displacement of thyronine analogs and thyronines from albumin and TBG by use of chem. blockers. A combination of 2 chem. blockers was used which eliminated thyronine analog-albumin binding but minimized thyronine displacement from TBG for use in FT4 and FT3 assays. These blocked-analog free-hormone assays yielded accurate clin. results in euthyroid patients, hypo- and hyperthyroid patients, and in pregnant women. FT4 results were not entirely normalized in all nonthyroidally ill patients, indicating that decreased analog-albumin binding is not the only factor resulting in low FT4 results. In current Diagnostic Products Corp. (DPC) FT4 and FT3 blocked-analog kits, the blocker concns. are the same as used in these assays.

L17 ANSWER 6 OF 7 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 3

AN 1988:143566 CAPLUS

DN 108:143566

TI Chemically blocked analog assays for free thyronines. I. The effect of chemical blockers on T4 analog and T4 binding by albumin and by **thyroxine**-binding globulin

AU Witherspoon, Lynn R.; **Shami, A. Said El**; Shuler, Stanton E.; Neely, Harold; Sonnemaker, Robert; Gilbert, Susan S.; Alyea, Kristin

CS Ochsner Clin., Alton Ochsner Med. Found., New Orleans, LA, 70121, USA

SO Clin. Chem. (Winston-Salem, N. C.) (1988), 34(1), 9-16
CODEN: CLCHAU; ISSN: 0009-9147

DT Journal

LA English

AB Analog assays for free **thyroxine** (FT4) produce inaccurate results because the T4 analog is sequestered by albumin. Diagnostic Products Corp. (DPC) introduced the concept of chem. blocking analog-albumin binding in 1982. Whereas DPC succeeded in

eliminating albumin dependence, their 1985 version of chem. blocked FT4 assay appeared to be **thyroxine**-binding globulin (TBG)-dependent, producing inappropriately low FT4 results with low TBG concns. and high results with high TBG concns. The effects of chem. blockers on albumin and TBG binding were examd. using equil. dialysis to measure free fractions of T4 analog and T4. FT4 assays were then created in which various concns. of chem. blockers were used to demonstrate their effects on FT4 ests. in patients with low or increased TBG concn. or who were pregnant. It was found that chem. blockers do displace T4 analog from albumin, but also displace T4 from albumin and, in high concns., from TBG as well. It is this displacement of T4 from TBG by chem. blockers that resulted in TBG dependence of DPC FT4 ests. This problem has been cor. in currently available versions of the DPC FT4 kit.

L17 ANSWER 7 OF 7 CAPLUS COPYRIGHT 1998 ACS DUPLICATE 4
AN 1987:436191 CAPLUS
DN 107:36191
TI Method for measuring free ligands in biological fluids
IN **El Shami, A. Said**
PA Diagnostic Products Corp., USA
SO Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 218309	A2	19870415	EP 86-300336	19860117
	EP 218309	A3	19880831		
	EP 218309	B1	19951115		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	EP 661540	A1	19950705	EP 95-103930	19860117
	EP 661540	B1	19980805		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	AT 130435	E	19951215	AT 86-300336	19860117
	AT 169410	E	19980815	AT 95-103930	19860117
	DK 8602196	A	19870405	DK 86-2196	19860512
	DK 169365	B1	19941010		
	AU 8657521	A1	19870409	AU 86-57521	19860516
	AU 602864	B2	19901101		
	ES 555425	A1	19870716	ES 86-555425	19860528
	CA 1299984	A1	19920505	CA 86-510762	19860604
	NO 8602278	A	19870406	NO 86-2278	19860606
	NO 168002	B	19910923		
	NO 168002	C	19920102		
	IL 79283	A1	19910630	IL 86-79283	19860630
	JP 62083666	A2	19870417	JP 86-157772	19860704
	JP 08001436	B4	19960110		

Devi, S.
09/036819

23dec98 11:46:38 User219783 Session D1433.2

SYSTEM:OS - DIALOG OneSearch
File 440:Current Contents Search(R) 1990-1998/Dec W2
(c) 1998 Inst for Sci Info
*File 440: Records starting 1997 to 1998W3 were reloaded, please note the changed in accession numbers.
File 144:Pascal 1973-1998/Nov
(c) 1998 INIST/CNRS
File 348:European Patents 1978-1998/Dec W51
(c) 1998 European Patent Office
*File 348: ** NEW FEATURE ** English language translations of French and German abstracts now searchable. See HELP NEWS 348 for info.
File 156:Toxline(R) 1965-1998/Nov
(c) format only 1998 The Dialog Corporation
File 484:Periodical Abstracts Plustext 1986-1998/Dec W1
(c) 1998 UMI
File 50:CAB Abstracts 1972-1998/Nov
(c) 1998 CAB International
File 35:Dissertation Abstracts Online 1861-1998/Dec
(c) 1998 UMI
File 98:General Sci Abs/Full-Text 1984-1998/Nov
(c) 1998 The HW Wilson Co.
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File 162:CAB HEALTH 1983-1998/Nov
(c) 1998 CAB INTERNATIONAL
File 444:New England Journal of Med. 1985-1998/Dec W4
(c) 1998 Mass. Med. Soc.
File 143:Biol. & Agric. Index 1983-1998/Nov
(c) 1998 The HW Wilson Co
File 357:Derwent Biotechnology Abs 1982-1998/Dec B3
(c) 1998 Derwent Publ Ltd
*File 357: Effective October 1, DialUnit rates adjusted for unrounding. See HELP NEWS 357 for details.
File 457:The Lancet 1986-1998/Dec W4
(c) 1998 The Lancet, Ltd.
File 10:AGRICOLA 70-1998/Dec
(c) format only 1998 The Dialog Corporation
File 99:Wilson Appl. Sci & Tech Abs 1983-1998/Nov
(c) 1998 The HW Wilson Co.
File 65:Inside Conferences 1993-1998/Dec W3
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File 129:PHIND(Archival) 1980-1998/Dec W3
(c) 1998 PJB Publications, Ltd.
File 229:Drug Info. 1998/98Q3
(c) 1998 Amer.Soc.of Health-Systems Pharm.

Set Items Description
Searcher : Shears 308-4994

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-key terms

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Set     Items   Description
S1        767   (THYROXINE OR TRIIODOTHYRONINE OR TRI(W)(IODOTHYRONINE OR -
              IODO(W)THYRONINE) OR TRIIODO(W)THYRONINE) AND LIGAND
S2        379   S1 AND (MEAS? OR QUANT? OR CALCUL?)
S3        483   S1 AND (DETECT? OR DETERM? OR DET??)
S4        221   (S2 OR S3) AND INCUB?
S5         31   S4 AND (DINITROPHENOL OR DI(W)(NITROPHENOL OR NITRO(W)PHEN-
              OL) OR DINITRO(W)PHENOL OR OLEIC OR SALICYLATE OR SULFOBROMOP-
              HTHALEIN OR SULPHOBROMOPHTHALEIN OR (SULFO OR SULPHO)(W)(BROM-
              OPHTHALEIN OR BROMO(W)PHTHALEIN))
S6         42   S1 AND (DINITROPHENOL OR DI(W)(NITROPHENOL OR NITRO(W)PHEN-
              OL) OR DINITRO(W)PHENOL OR OLEIC OR SALICYLATE OR SULFOBROMOP-
              HTHALEIN OR SULPHOBROMOPHTHALEIN OR (SULFO OR SULPHO)(W)(BROM-
              OPHTHALEIN OR BROMO(W)PHTHALEIN))
S7         42   S5 OR S6
S8         36   RD (unique items)
? t 8/3,ab/1-36

>>>No matching display code(s) found in file(s): 65, 129, 229

 8/3,AB/1      (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
(c) 1998 Inst for Sci Info. All rts. reserv.

08505038   GENUINE ARTICLE#: XC375   NUMBER OF REFERENCES: 32
TITLE: Pulsed ultrafiltration mass spectrometry: A new method for screening
    combinatorial libraries
AUTHOR(S): vanBreemen RB (REPRINT); Huang CR; Nikolic D; Woodbury CP; Zhao
    YZ; Venton DL
CORPORATE SOURCE: UNIV ILLINOIS,COLL PHARM, DEPT MED CHEM & PHARMACOGNOSY,
    833 S WOOD ST, M-C 781/CHICAGO//IL/60612 (REPRINT)
PUBLICATION TYPE: JOURNAL
PUBLICATION: ANALYTICAL CHEMISTRY, 1997, V69, N11 (JUN 1), P2159-2164
PUBLISHER: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036
ISSN: 0003-2700
LANGUAGE: English   DOCUMENT TYPE: ARTICLE
ABSTRACT: In response to the need for rapid screening of combinatorial
    libraries to identify new lead compounds during drug discovery, we have
    developed an on-line combination of ultrafiltration and electrospray
    mass spectrometry, called pulsed ultrafiltration mass spectrometry,
    which facilitates the identification of solution-phase ligands in
    library mixtures that bind to solution-phase receptors. After ligands
    contained in a library mixture were bound to a macromolecular receptor,
    e.g., human serum albumin or calf intestine adenosine deaminase, the
    ligand-receptor complexes were purified by ultrafiltration and
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then dissociated using methanol to elute the ligands into the electrospray mass spectrometer for detection. Ligands with dissociation constants in the micromolar to nanomolar range were successfully bound, released, and detected using this method, including warfarin, **salicylate**, furosemide, and **thyroxine** binding to human serum albumin, and erythro-9-(2-hydroxy-3-nonyl)adenine binding to calf intestine adenosine deaminase. Repetitive bind-and-release experiments demonstrated that the receptor could be reused, Thus, pulsed ultrafiltration mass spectrometry was shown to provide a simple and powerful new method for the screening of combinatorial libraries in support of new drug discovery.

ISSN: 0003-2700

8/3,AB/2 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

08778857 PASCAL No.: 89-0328159

Is **oleic** acid the **thyroxine** binding inhibitor in the serum of ill patients?

HAYNES I G; LOCKETT S J; FARMER M J; FITCH N J; BRADWELL A R; SHEPPARD M C; RAMSDEN D B

Univ. Birmingham, dep. medicine, Birmingham B15 2TH, United Kingdom

Journal: Clinical endocrinology (Oxford), 1989, 31 (1) 25-30

Language: English

The objectif of this work is to explore the hypothesis that **oleic** acid is the T4 binding inhibitor that is present in severly ill patients who had reduced TT4 concentrations. Two aspects of this hypothesis are investigated. Firstly, evidence of a direct interaction between **oleic** acid and TBG was sought (binding study, using the techniques of one and two dimensional immunoelectrophoresis and autoradiography) and secondly, correlations between TT4 concentrations and **oleic** acid concentrations in two groups of patients

8/3,AB/3 (Item 1 from file: 348)
DIALOG(R)File 348:European Patents

00923312

ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348

Human telomerase catalytic subunit

Katalytische Untereinheit der menschlichen Telomerase

Sous-unite catalytique de la telomerase humaine

PATENT ASSIGNEE:

Geron Corporation, (1733111), 230 Constitution Drive, Menlo Park, CA 94025, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FI;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)

University Technology Corporation, (2274850), Suite 250, 3101 Iris Avenue , Boulder, CO 80301, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FI;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
INVENTOR:
Cech, Thomas R., 1545 Rockmount Circle, Boulder Colorado 80303, (US)
Lingner, Joachim, 360-30th Street, Boulder Colorado 80303, (US)
Nakamura, Toru, 4940 Thunderbird Circle, 204, Boulder Colorado 80303, (US)
Chapman, Karen B., 71 Cloud View Road, Sausalito California 94965, (US)
Morin, Cregg B., 3407 Janice Way, Palo Alto California 94303, (US)
Harley, Calvin, 1730 University Avenue, Palo Alto California 94301, (US)
Andrews, William H., 6102 Park Avenue, Richmond California 94085, (US)
LEGAL REPRESENTATIVE:
Bizley, Richard Edward et al (28352), Hepworth, Lawrence, Bryer & Bizley Merlin House Falconry Court Baker's Lane, Epping Essex CM16 5DQ, (GB)
PATENT (CC, No, Kind, Date): EP 841396 A1 980513 (Basic)
APPLICATION (CC, No, Date): EP 97307757 971001;
PRIORITY (CC, No, Date): US 724643 961001; US 844419 970418; US 846017 970425; US 851843 970506; US 854050 970509; US 911312 970814; US 912951 970814; US 915503 970814
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/54; C12N-009/12; C12Q-001/68; C12Q-001/48; C12N-015/11; C12N-015/85; A01K-067/027; C07K-016/40; A61K-038/45; A61K-031/70; C12N-001/21; C12N-001/19;

ABSTRACT EP 841396 A1
The invention provides compositions and methods related to human telomerase reverse transcriptase (hTRT), the catalytic protein subunit of human telomerase. The polynucleotides and polypeptides of the invention are useful for diagnosis, prognosis and treatment of human diseases, for changing the proliferative capacity of cells and organisms, and for identification and screening of compounds and treatments useful for treatment of diseases such as cancers.
ABSTRACT WORD COUNT: 64

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9820	968
SPEC A	(English)	9820	83027
Total word count - document A			83995
Total word count - document B			0
Total word count - documents A + B			83995

8/3,AB/4 (Item 2 from file: 348)
DIALOG(R)File 348:European Patents

00711505
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Cyclosporin immunoassay.
Cyclosporin-Immunoassay.
Essai immunologique de cyclosporine.
PATENT ASSIGNEE:
SYNTEX (U.S.A.) INC., (200863), 3401 Hillview Avenue, Palo Alto California 94304, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Davalian, Dariush, 5363 Romford Drive, San Jose, CA 95124, (US)
Alexander, Svetlana, 913 Hollenbeck Avenue, Sunnyvale, CA 94087, (US)
Ullman, Edwin F., 135 Selby Lane, Atherton, CA 94025, (US)
Beresini, Maureen H., 821 Kelmore Street, Moss Beach, CA 94038, (US)
Hu, Mae W., 26705 St Francis, Los Atlos Hills, CA 94022, (US)
LEGAL REPRESENTATIVE:
Armitage, Ian Michael et al (27761), MEWBURN ELLIS York House 23 Kingsway , London WC2B 6HP, (GB)
PATENT (CC, No, Kind, Date): EP 674178 A2 950927 (Basic)
EP 674178 A3 960710
APPLICATION (CC, No, Date): EP 95108148 911119;
PRIORITY (CC, No, Date): US 616116 901120
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: G01N-033/68; G01N-033/541; G01N-033/58; C07K-007/64; C07K-016/44;

ABSTRACT EP 674178 A3
A method of inactivating interfering cross-reactive material in an assay for **measuring** the amount of cyclosporin in a sample suspected of containing cyclosporin is also disclosed. Compositions wherein cyclosporin is conjugated to an immunogenic carrier or a label, optionally through a linking group, at an alanine nitrogen atom of the cyclic backbone of cyclosporin are also disclosed. Compositions wherein atiocyclosporin is conjugated, optionally through a linking group, to an immunogenic carrier or a label are also disclosed. Where cyclosporin is conjugated to an immunogenic carrier, the conjugates may be used as immunogens for the preparation of antibodies which are capable of recognizing cyclosporin. Where atiocyclosporin is conjugated to an immunogenic carrier, the conjugates may be used as immunogens for the preparation of antibodies which are capable of recognizing interfering cross-reactive material but substantially incapable of recognizing cyclosporin or cyclosporin-label conjugates. Where cyclosporin is conjugated to a label, the conjugates may be used as part of a signal producing system in cyclosporin assays. Both the antibodies and label conjugates are useful in the disclosed assay methods.
ABSTRACT WORD COUNT: 204

LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPAB95	599
SPEC A	(English)	EPAB95	21779
Total word count - document A			22378
Total word count - document B			0
Total word count - documents A + B			22378

8/3,AB/5 (Item 3 from file: 348)
DIALOG(R)File 348:European Patents

00694807
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Method for **measuring** free testosterone in biological fluids
Verfahren zum Messen von Freitestosteronen in biologischen Flussigkeiten
Methode pour **determiner** les testosterones libres dans les fluides biologiques

PATENT ASSIGNEE:
DIAGNOSTIC PRODUCTS CORPORATION, (728210), 5700 West 96th Street, Los Angeles California 90045, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:
Said el Shami, A. Dr. Diagnostic Products Corp., 5700 West 96th Street, Los Angeles, Ca 90045, (US)
LEGAL REPRESENTATIVE:
Goldin, Douglas Michael (31061), J.A. KEMP & CO. 14 South Square Gray's Inn, London WC1R 5LX, (GB)

PATENT (CC, No, Kind, Date): EP 661540 A1 950705 (Basic)
EP 661540 B1 980805
APPLICATION (CC, No, Date): EP 95103930 860117;
PRIORITY (CC, No, Date): US 784857 851004
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: G01N-033/74; G01N-033/543; G01N-033/545;

ABSTRACT EP 661540 A1

The invention provides a method for **measuring** the concentration of free testosterone **ligand** in a biological fluid in the presence of bound **ligand** and endogenous binding proteins, without disturbing the equilibrium between free **ligand** and protein-bound **ligand**, which method comprises

(a) **incubating**, in the absence of **salicylate**, 2,4-**dinitrophenol** and 8-anilino-1-naphthalenesulfonic acid, a sample of the biological fluid with (i) a **ligand** analog tracer which, due to its chemical structure, does not bind to some of the endogenous binding proteins but does bind to at least one other endogenous binding protein, (ii) a concentration of a specific **ligand** binder having an affinity constant and selectivity for the free **ligand** such that the

equilibrium between free **ligand** and protein-bound **ligand** is not disturbed and (iii) a concentration of **sulfobromophthalein** (SBP) that inhibits the binding of the **ligand** analog tracer to said at least one other endogenous binding protein sufficient to block reaction between the **ligand** analog tracer and said at least one other endogenous binding protein without displacing **ligand** from protein-bound **ligand**;

(b) separating the **ligand** analog tracer bound to the specific **ligand** binder from unbound tracer; and

(c) **determining** the concentration of free **ligand** in said biological fluid.

ABSTRACT WORD COUNT: 201

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9832	379
CLAIMS B	(German)	9832	360
CLAIMS B	(French)	9832	426
SPEC B	(English)	9832	2790
Total word count - document A			0
Total word count - document B			3955
Total word count - documents A + B			3955

8/3,AB/6 (Item 4 from file: 348)
DIALOG(R)File 348:European Patents

00565191
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Method for the **quantitative determination** of a free form of substances present in biological fluids.
Verfahren zur **quantitation** Bestimmung einer freien Form einer Substanz in biologischen Flussigkeiten.
Procede pour la **determination quantitative** d'une forme libre d'une substance dans des liquides biologiques.
PATENT ASSIGNEE:
TECHNOGENETICS S.r.l., (873221), Via M. Civitali, 1, I-20148 Milano, (IT) , (applicant designated states: BE;DE;ES;FR;GB;IT)
INVENTOR:
Romelli, Pier Bruno, Via Perfetti, 1, I-20017 Rho, Milan, (IT)
Chiodoni, Giovanni, Via Monte Grappa, 19, I-20069 Vaprio d'Adda, Varese, (IT)
Ringhini, Roberto, Via Carducci, 1/D, I-20060 Cassina de 'Pecchi, Milan, (IT)
LEGAL REPRESENTATIVE:
Gervasi, Gemma et al (40513), NOTARBARTOLO & GERVASI Srl Viale Bianca Maria 33, I-20122 Milan, (IT)

PATENT (CC, No, Kind, Date): EP 565949 A2 931020 (Basic)
EP 565949 A3 940105
APPLICATION (CC, No, Date): EP 93105327 930331;
PRIORITY (CC, No, Date): IT 92MI910 920414
DESIGNATED STATES: BE; DE; ES; FR; GB; IT
INTERNATIONAL PATENT CLASS: G01N-033/78; G01N-033/543

ABSTRACT EP 565949 A2
Disclosed is a method for **determining** the free fraction of analytes present in biological fluids in a free form which is in equilibrium with a form bound to one or more endogenous ligands. This method comprises:
a) contacting the biological fluid with a first exogenous **ligand** L1, capable of sequestering an analyte **quantity** proportionate to said free-fraction;
b) contacting the L1/analyte complex so obtained, preferably after removal from the biological fluid of the endogenous **ligand**, with a dissociating agent able to dissociate the sequestered analyte, and with a labelled analyte, in the presence of a second **ligand** capable of binding both the dissociated and the labelled analyte;
c) **measuring** the **quantity** of the either bound or unbound labelled analyte .
ABSTRACT WORD COUNT: 124

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	715
SPEC A	(English)	EPABF1	6618
Total word count - document A			7333
Total word count - document B			0
Total word count - documents A + B			7333

8/3,AB/7 (Item 5 from file: 348)
DIALOG(R)File 348:European Patents

00538609
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Immunoassay for immunoglubulins.
Immunoassay zum nachweis von Immunoglobulinen.
Essai immunologique pour **determiner** des immunoglobulines.
PATENT ASSIGNEE:
SYNTEX (U.S.A.) INC., (200863), 3401 Hillview Avenue, Palo Alto California 94304, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;PT;SE)
INVENTOR:
Rejman, John J., 13619 Highway 70 East, Lenior City TN 37771, (US)
Searcher : Shears 308-4994

Weng, Litai, 995 N. California Avenue, Palo Alto CA 94303, (US)
Varro, Rudolph, 3402 Woodstock Lane, Mt. View CA 94040, (US)
LEGAL REPRESENTATIVE:
Nicholls, Kathryn Margaret et al (60341), MEWBURN ELLIS York House 23 Kingsway, London WC2B 6HP, (GB)
PATENT (CC, No, Kind, Date): EP 507587 A2 921007 (Basic)
EP 507587 A3 930303
APPLICATION (CC, No, Date): EP 92302913 920402;
PRIORITY (CC, No, Date): US 679693 910403
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; PT; SE
INTERNATIONAL PATENT CLASS: G01N-033/68; G01N-033/576; G01N-033/543

ABSTRACT EP 507587 A2
A method for carrying out an immunoassay for an immunoglobulin in which a sample suspected of containing the immunoglobulin and reagents useful for **detecting** the immunoglobulin of interest are combined in a single step in an aqueous medium, wherein one of the reagents includes a small molecule bound to a receptor for the immunoglobulin, one includes an antigen capable of binding to the immunoglobulin and one includes a signal generating means bound to a receptor for the antigen capable of binding to a site on the antigen different from the site of binding of the immunoglobulin.
ABSTRACT WORD COUNT: 98

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	783
SPEC A	(English)	EPABF1	7589
Total word count - document A			8372
Total word count - document B			0
Total word count - documents A + B			8372

8/3,AB/8 (Item 6 from file: 348)
DIALOG(R)File 348:European Patents

00538608

Immunoassay for immunoglobulins.
Immunoassay zum Bachweis von Immunoglobulinen.
Essai immunologique pour **determiner** des immunoglobulines.
PATENT ASSIGNEE:
SYNTEX (U.S.A.) INC., (200863), 3401 Hillview Avenue, Palo Alto California 94304, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;PT;SE)
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PATENT (CC, No, Kind, Date): EP 507586 A2 921007 (Basic)
EP 507586 A3 930303
APPLICATION (CC, No, Date): EP 92302912 920402;
PRIORITY (CC, No, Date): US 679270 910403
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; PT; SE
INTERNATIONAL PATENT CLASS: G01N-033/68; G01N-033/576; G01N-033/543

ABSTRACT EP 507586 A2
A method for carrying out an immunoassay for an immunoglobulin in which a sample suspected of containing the immunoglobulin and reagents useful for **detecting** the immunoglobulin of interest are combined in a single step in an aqueous medium, wherein one of the reagents includes a small molecule bound to a first antigen capable of binding to the immunoglobulin and another includes a signal generating means bound to a second antigen capable of binding to the immunoglobulin.
ABSTRACT WORD COUNT: 78

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	683
SPEC A	(English)	EPABF1	7681
Total word count - document A			8364
Total word count - document B			0
Total word count - documents A + B			8364

8/3,AB/9 (Item 7 from file: 348)
DIALOG(R)File 348:European Patents

00489828
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Cyclosporin immunoassay
Immunotest fur Cyclosporin
Immunoessai pour cyclosporine
PATENT ASSIGNEE:
BEHRINGWERKE Aktiengesellschaft, (201590), Postfach 1140, 35001 Marburg, (DE), (applicant designated states:
AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
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Searcher : Shears 308-4994

Beresini, Maureen H., 821 Kelmore Street, Moss Beach, CA 94038, (US)
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Hu, Mae W., 26705 St. Francis, Los Atlos Hill, CA 94022, (US)
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LEGAL REPRESENTATIVE:
Nicholls, Kathryn Margaret et al (60341), MEWBURN ELLIS York House 23 Kingsway, London WC2B 6HP, (GB)
PATENT (CC, No, Kind, Date): EP 487289 A2 920527 (Basic)
EP 487289 A3 940223
EP 487289 B1 960904
APPLICATION (CC, No, Date): EP 91310632 911119;
PRIORITY (CC, No, Date): US 616116 901120
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: G01N-033/68; G01N-033/531; G01N-033/535; C07K-007/64; C07K-016/44;

ABSTRACT EP 487289 A2

A method of **measuring** the amount of cyclosporin in a sample suspected of containing cyclosporin is disclosed. A method of inactivating interfering cross-reactive material in an assay for **measuring** the amount of cyclosporin in a sample suspected of containing cyclosporin is also disclosed. Compositions wherein cyclosporin is conjugated to an immunogenic carrier or a label, optionally through a linking group, at an alanine nitrogen atom of the cyclic backbone of cyclosporin are also disclosed. Compositions wherein atiocyclosporin is conjugated, optionally through a linking group, to an immunogenic carrier or a label are also disclosed. Where cyclosporin is conjugated to an immunogenic carrier, the conjugates may be used as immunogens for the preparation of antibodies which are capable of recognizing cyclosporin. Where atiocyclosporin is conjugated to an immunogenic carrier, the conjugates may be used as immunogens for the preparation of antibodies which are capable of recognizing interfering cross-reactive material but substantially incapable of recognizing cyclosporin or cyclosporin-label conjugates. Where cyclosporin is conjugated to a label, the conjugates may be used as part of a signal producing system in cyclosporin assays. Both the antibodies and label conjugates are useful in the disclosed assay methods.
ABSTRACT WORD COUNT: 194

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	1285
CLAIMS B	(English)	EPAB96	715
CLAIMS B	(German)	EPAB96	730
CLAIMS B	(French)	EPAB96	779
SPEC A	(English)	EPABF1	21924
SPEC B	(English)	EPAB96	18420
Total word count - document A			23211

Searcher : Shears 308-4994

Total word count - document B 20644
Total word count - documents A + B 43855

8/3,AB/10 (Item 8 from file: 348)
DIALOG(R)File 348:European Patents

00485827
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Method producing a polynucleotide for use in single primer amplification
Verfahren zur Herstellung eines Polynukleotides zur Verwendung bei Einzelprimeramplifikation
Procede de production d'un polynucleotide pour utilisation dans une amplification a l'aide d'une seule amorce
PATENT ASSIGNEE:
BEHRINGWERKE Aktiengesellschaft, (201590), Postfach 1140, 35001 Marburg, (DE), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
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Becker, Martin, 3481 Greer Road, Palo Alto, CA 94303, (US)
Ullman, Edwin F., 135 Selby Lane, Atherton, CA 94025, (US)
LEGAL REPRESENTATIVE:
Nicholls, Kathryn Margaret et al (60341), MEWBURN ELLIS York House 23 Kingsway, London WC2B 6HP, (GB)
PATENT (CC, No, Kind, Date): EP 469755 A1 920205 (Basic)
EP 469755 B1 961002
APPLICATION (CC, No, Date): EP 91306550 910718;
PRIORITY (CC, No, Date): US 555323 900719
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12P-019/34; C12Q-001/68;

ABSTRACT EP 469755 A1
A method is disclosed for producing a single stranded polydeoxynucleotide having two segments that are non-contiguous and complementary with each other. The method comprises the steps of providing in combination (1) a polynucleotide having two non-contiguous, non-complementary nucleotide sequences S1 and S2 wherein S2 is 5(min) of S1 and is at least ten deoxynucleotides long and (2) an extender probe comprised of two deoxynucleotide sequences, wherein the sequence at the 3(min)-end of the extender probe is hybridizable with S1 and the other of the deoxynucleotide sequences is homologous to S2 and (b) extending the extender probe along the polynucleotide. The method can also comprise providing in the combination a polydeoxynucleotide primer capable of hybridizing at least at its 3(min)-end with a nucleotide sequence complementary to S2 under conditions where (1) the extended extender probe is rendered single stranded, (2) the polydeoxynucleotide primer

hybridizes with and is extended along the extended extender probe to form a duplex comprising extended primer, (3) the extended primer is dissociated from the duplex, and (4) the primer hybridizes with and is extended along the extended primer to form a duplex comprising extended primer, and repeating steps (3) and (4). The method finds particular application in the **detection** of polynucleotide analytes.
ABSTRACT WORD COUNT: 207

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	1455
CLAIMS B	(English)	EPAB96	1463
CLAIMS B	(German)	EPAB96	1401
CLAIMS B	(French)	EPAB96	1622
SPEC A	(English)	EPABF1	12457
SPEC B	(English)	EPAB96	12366
Total word count - document A			13913
Total word count - document B			16852
Total word count - documents A + B			30765

8/3,AB/11 (Item 9 from file: 348)
DIALOG(R)File 348:European Patents

00464071
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
An analyte-subtitute reagent for use in specific binding assay methods, devices and kits
Analyt-Austauschreagenz zur Verwendung in spezifischen Bindungstests, -vorrichtungen und -satzen
Reactif a base de substitution d'une analyte a utiliser dans les essais, les dispositifs et les trousses de liaisons specifiques
PATENT ASSIGNEE:
ABBOTT LABORATORIES, (225073), One Abbott Park Road, Abbott Park, Illinois 60064-3500, (US), (applicant designated states: DE;ES;FR;IT)
INVENTOR:
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Chamberlain, Aurora J., 11 University Court, Buffalo Grove, IL 60089, (US)
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LEGAL REPRESENTATIVE:
Modiano, Guido, Dr.-Ing. et al (40782), Modiano & Associati S.r.l. Via Meravigli, 16, I-20123 Milano, (IT)
PATENT (CC, No, Kind, Date): EP 467078 A2 920122 (Basic)
EP 467078 A3 920506
EP 467078 B1 960508
Searcher : Shears 308-4994

APPLICATION (CC, No, Date): EP 91109936 910618;
PRIORITY (CC, No, Date): US 554304 900718
DESIGNATED STATES: DE; ES; FR; IT
INTERNATIONAL PATENT CLASS: G01N-033/53; G01N-033/543;

ABSTRACT EP 467078 A2
Assay reagents, devices, methods and kits used in the analysis of low molecular weight analytes which by themselves are too small or unable to bind to two specific binding members at the same time. The invention involves the use of an analyte-substitute reagent (ASR) comprising at least two components, the first of which is identical to or an analog of the analyte to be **determined**, while the second is an unrelated **ligand** for which an antibody or other specific binding member can be obtained or produced.
ABSTRACT WORD COUNT: 88

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	791
CLAIMS B	(English)	EPAB96	616
CLAIMS B	(German)	EPAB96	592
CLAIMS B	(French)	EPAB96	824
SPEC A	(English)	EPABF1	10793
SPEC B	(English)	EPAB96	10681
Total word count - document A			11585
Total word count - document B			12713
Total word count - documents A + B			24298

8/3,AB/12 (Item 10 from file: 348)
DIALOG(R)File 348:European Patents

00461819
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Barbiturate assay, tracers, immunogens, antibodies and kit
Test fur Barbiturate, Tracer, Immunogene, Antikorper und Testsatz dafur
Essai pour barbiturates, traceurs, immunogenes, anticorps et trousse
PATENT ASSIGNEE:
ABBOTT LABORATORIES, (225073), One Abbott Park Road, Abbott Park, Illinois 60064-3500, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;IT;LI;NL)
INVENTOR:
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Dubler, Robert Edward, 5041 Adele Drive, Gurnee, IL 60031, (US)
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PATENT (CC, No, Kind, Date): EP 457213 A2 911121 (Basic)
EP 457213 A3 920902
EP 457213 B1 970723
APPLICATION (CC, No, Date): EP 91107624 910510;
PRIORITY (CC, No, Date): US 524195 900516
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; IT; LI; NL
INTERNATIONAL PATENT CLASS: G01N-033/94; G01N-033/542; G01N-033/532; G01N-033/533; C07D-405/12; C07D-493/10; C07D-493/10; C07D-311/00; C07D-307/00

ABSTRACT EP 457213 A2
The present invention is directed to a fluorescence polarization immunoassay for barbiturates, to the various components needed for preparing and carrying out such an assay, and to methods of making these components. Specifically, tracers, immunogens and antibodies are disclosed, as well as methods for preparing them and a reagent kit containing them. The tracers and the immunogens are made from substituted barbiturate compounds. A fluorescein moiety is included in the tracer, while a poly(amino acid) forms a part of the immunogen. The assay is conducted by **measuring** the degree of polarization retention of plane-polarized light that has been passed through a sample containing antiserum and tracer. (see image in original document)
ABSTRACT WORD COUNT: 113
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	719
CLAIMS B	(English)	9707W4	2531
CLAIMS B	(German)	9707W4	2506
CLAIMS B	(French)	9707W4	2737
SPEC A	(English)	EPABF1	14114
SPEC B	(English)	9707W4	14201
Total word count - document A			14835
Total word count - document B			21975
Total word count - documents A + B			36810

8/3,AB/13 (Item 11 from file: 348)
DIALOG(R)File 348:European Patents

00436175
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Improvement in non-instrumental diagnostic assay distance **determination**.

Searcher : Shears 308-4994

Verbesserung in einem geratefreien auf Entfernungsbestimmung beruhenden diagnostischen Test.
Amelioration dans un essai diagnostique non-instrumental d'une **determination** a distance.

PATENT ASSIGNEE:
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INVENTOR:
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PATENT (CC, No, Kind, Date): EP 427534 A1 910515 (Basic)
EP 427534 B1 950802
APPLICATION (CC, No, Date): EP 90312183 901107;
PRIORITY (CC, No, Date): US 433538 891108
DESIGNATED STATES: DE; GB
INTERNATIONAL PATENT CLASS: G01N-033/558; G01N-033/92

ABSTRACT EP 427534 A1

In assays providing for **measurement** of the analyte based on the length of a region producing a **detectable** signal, results may be improved by providing for a region which is relatively small and captures either analyte or a component of a reagent system producing a **detectable** signal, where the amount of the component is related to the amount of analyte. Particularly, a narrow band is provided of concentrated dye which reacts with hydrogen peroxide in a cholesterol assay, so that the dynamic range which is **measured** may be expanded providing for higher sensitivity, shorter wicking distances, and shorter times for wicking.

ABSTRACT WORD COUNT: 105

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPAB95	430
CLAIMS B	(German)	EPAB95	412
CLAIMS B	(French)	EPAB95	510
SPEC B	(English)	EPAB95	7643
Total word count - document A			0
Total word count - document B			8995
Total word count - documents A + B			8995

8/3,AB/14 (Item 12 from file: 348)
DIALOG(R)File 348:European Patents

00420627
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Stabilization of monoclonal antibody for use in fluorescent polarization techniques.
Stabilisierung von monoklonalen Antikorpern zur Verwendung in Fluoreszenz-Polarisierungsmethoden.
Stabilisation d'anticorps monoclonaux pour utiliser dans les techniques de polarisation de fluorescence.
PATENT ASSIGNEE:
ABBOTT LABORATORIES, (225073), CHAD-0377, AP6D/2, One Abbott Park Road, Abbott Park, Illinois 60064-3500, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;IT;LI;NL)
INVENTOR:
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Flentge, Charles A., 37338 Fairview Lane, Lake Villa, Illinois 60046, (US)
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LEGAL REPRESENTATIVE:
Modiano, Guido et al (40782), MODIANO, JOSIF, PISANTY & STAUB Modiano & Associati Via Meravigli, 16, I-20123 Milano, (IT)
PATENT (CC, No, Kind, Date): EP 420102 A2 910403 (Basic)
EP 420102 A3 920304
APPLICATION (CC, No, Date): EP 90118309 900924;
PRIORITY (CC, No, Date): US 414177 890928
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; IT; LI; NL
INTERNATIONAL PATENT CLASS: G01N-033/58; G01N-033/577;

ABSTRACT EP 420102 A2
A method for **determining** ligands in a sample is disclosed. The method involves mixing with the sample in which the **ligand** is to be **determined** a tracer having the formula of Fig. 1 of the attached drawings or a biologically acceptable salt of such a tracer, a monoclonal antibody, and glycerol added as a part of a solution of the monoclonal antibody in which the glycerol is present in an amount sufficient to increase the stability of the monoclonal antibody in the solution, and then **determining** the amount of tracer bound to the antibody by fluorescence polarization techniques as a **measure** of the amount of **ligand** in the sample. In Fig. 1 of the drawings R is a **ligand** or analog thereof having at least one common epitope with a **ligand** to be **determined** so that the **ligand** to be **determined** and the **ligand** or analog thereof of the tracer are both specifically recognizable by a given antibody, and N is an integer from one to ten. The monoclonal antibody used is one which is capable of

specifically recognizing both the **ligand** to be **determined** and the tracer. Glycerol is used in the monoclonal antibody solution in an amount, usually from about 5 percent to about 20 percent, sufficient to increase the stability of the monoclonal antibody. The optimum glycerol concentration has been found to be about 10%. (see image in original document)
ABSTRACT WORD COUNT: 237

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	411
SPEC A	(English)	EPABF1	2281
Total word count - document A			2692
Total word count - document B			0
Total word count - documents A + B			2692

8/3,AB/15 (Item 13 from file: 348)
DIALOG(R)File 348:European Patents

00396949
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Nucleic acid amplification using single primer
Nukleinsaure-Amplifikation unter Verwendung eines Einzelprimers
Amplification d'acides nucleiques utilisant une amorce
PATENT ASSIGNEE:
BEHRINGWERKE Aktiengesellschaft, (201590), Postfach 1140, 35001 Marburg, (DE), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
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Western, Linda M., 1725 Wright Avenue Nr. 18, Mountain View, CA 94043, (US)
Becker, Martin, 3481 Greer Road, Palo Alto, CA 94303, (US)
Ullman, Edwin F., 135 Selby Lane, Atherton, CA 94025, (US)
LEGAL REPRESENTATIVE:
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PATENT (CC, No, Kind, Date): EP 379369 A2 900725 (Basic)
EP 379369 A3 910703
EP 379369 B1 960904
APPLICATION (CC, No, Date): EP 90300528 900118;
PRIORITY (CC, No, Date): US 299282 890119; US 399795 890829
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12Q-001/68;

ABSTRACT EP 379369 A2

A method is disclosed for **determining** the presence of a polynucleotide analyte in a sample suspected of containing the analyte. The method comprises (a) forming as a result of the presence of an analyte a single stranded polynucleotide comprising a target polynucleotide binding sequence flanked by first and second polynucleotide sequences that differ from the sequence of the analyte or a sequence complementary to the analyte sequence, (b) forming multiple copies of the single stranded polynucleotide, and (c) **detecting** the single stranded polynucleotide. Also disclosed is a method of producing at least one copy of a single stranded polynucleotide. The method comprises (a) forming in the presence of nucleoside triphosphates and template dependent polynucleotide polymerase an extension of a polynucleotide primer at least the 3(min)-end of which has at least a 10 base sequence hybridizable with a second sequence flanking the 3(min)-end of the single stranded polynucleotide, the second sequence being partially or fully complementary with at least a 10 base first sequence flanking the 5(min) end of the single stranded polynucleotide, (b) dissociating the extended polynucleotide primer and the single stranded polynucleotide, (c) repeating step a and (d) dissociating the extended polynucleotide primer and the copy of the single stranded polynucleotide.

ABSTRACT WORD COUNT: 206

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	2100
CLAIMS B	(English)	EPAB96	2072
CLAIMS B	(German)	EPAB96	1992
CLAIMS B	(French)	EPAB96	2380
SPEC A	(English)	EPABF1	15325
SPEC B	(English)	EPAB96	14976
Total word count - document A			17426
Total word count - document B			21420
Total word count - documents A + B			38846

8/3,AB/16 (Item 14 from file: 348)
DIALOG(R)File 348:European Patents

00396727
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Threshold ligand-receptor assay.
Liganden-Rezeptor-Assays unter Verwendung eines Schwellenwertes.
Des essais ligands-recepteurs utilisant un seuil.
PATENT ASSIGNEE:
BIOSITE DIAGNOSTICS INC., (1184930), 10955 John Jay Hopkins Drive, San

Diego California 92121, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)

INVENTOR:
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LEGAL REPRESENTATIVE:
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PATENT (CC, No, Kind, Date): EP 378391 A2 900718 (Basic)
EP 378391 A3 911002
EP 378391 B1 950913

APPLICATION (CC, No, Date): EP 90300283 900110;

PRIORITY (CC, No, Date): US 295568 890110

DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE

INTERNATIONAL PATENT CLASS: G01N-033/50; G01N-033/541; G01N-033/543; G01N-033/74; G01N-033/94

ABSTRACT EP 378391 A2

This invention is directed to a ligand-receptor assay for determining the presence or amount of at least one target ligand, capable of competing with a ligand analogue conjugate for binding sites available on a ligand receptor, said ligand analogue conjugate comprising at least one ligand analogue coupled to a signal development element capable of emitting a detectable signal, in a fluid sample suspected of containing said target ligand, comprising the steps of:

a. contacting said fluid sample with ligand analogue conjugate and ligand receptor to form a reaction mixture, the relative amounts of ligand analogue conjugate and ligand receptor being such that in the absence of target ligand, and subsequent to substantially equilibrium binding, substantially all of the ligand analogue conjugate is bound to ligand receptor;

b. detecting the unbound ligand analogue conjugate;

c. relating the detectable signal to the presence or amount of target ligand in the fluid sample. In one embodiment an optional means also is employed for removing receptor from the reaction mixture. In related claimed assay formats the analyte of interest may be either ligand receptor or ligand.

ABSTRACT WORD COUNT: 188

LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	1943
CLAIMS B	(English)	EPAB95	2359
CLAIMS B	(German)	EPAB95	2094
CLAIMS B	(French)	EPAB95	2829

Searcher : Shears 308-4994

SPEC A	(English)	EPABF1	20425
SPEC B	(English)	EPAB95	20380
Total word count - document A			22370
Total word count - document B			27662
Total word count - documents A + B			50032

8/3,AB/17 (Item 15 from file: 348)
DIALOG(R)File 348:European Patents

00368701
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Method for **detection** of specific nucleic acid sequences.
Verfahren zum Nachweis spezifischer Nukleinsauresequenzen.
Methode de **detection** de sequences specifiques d'acide nucleique.
PATENT ASSIGNEE:
SYNTEX (U.S.A.) INC., (200862), 3401 Hillview Avenue P.O. Box 10850, Palo Alto California 94303, (US), (applicant designated states: DE;FR;GB)
INVENTOR:
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Stull, Paul D., 2101 California Avenue, Nr. 225 Mountain View California 94040, (US)
LEGAL REPRESENTATIVE:
Armitage, Ian Michael et al (27761), MEWBURN ELLIS York House 23 Kingsway , London WC2B 6HP, (GB)
PATENT (CC, No, Kind, Date): EP 357336 A2 900307 (Basic)
EP 357336 A3 910227
EP 357336 B1 941005
APPLICATION (CC, No, Date): EP 89308577 890824;
PRIORITY (CC, No, Date): US 236967 880825
DESIGNATED STATES: DE; FR; GB
INTERNATIONAL PATENT CLASS: C12Q-001/68;

ABSTRACT EP 357336 A2
A method is disclosed for **detecting** the presence of a target nucleotide sequence in a polynucleotide. The method comprises hybridizing a first nucleotide sequence and a second nucleotide sequence to non-contiguous portions of a target nucleotide sequence, covalently attaching the first and second sequences when they are hybridized to the target sequence, and **determining** the presence of covalently attached first and second sequences. The presence of the covalently attached first and second sequences is related to the presence of the target nucleotide sequence. The invention may be applied to target nucleotide sequences in DNA or RNA. Specific target nucleotide sequences of interest will frequently be characteristic of particular microorganisms, viruses, viroids, or genetic characteristics, including

genetic abnormalities.
ABSTRACT WORD COUNT: 121

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPBBF1	1441
CLAIMS B	(English)	EPBBF1	380
CLAIMS B	(German)	EPBBF1	356
CLAIMS B	(French)	EPBBF1	445
SPEC A	(English)	EPBBF1	12216
SPEC B	(English)	EPBBF1	10838
Total word count - document A			13657
Total word count - document B			12019
Total word count - documents A + B			25676

8/3,AB/18 (Item 16 from file: 348)
DIALOG(R)File 348:European Patents

00366528
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Multiparameter particle analysis.
Teilchenanalyse auf mehrere Parameter.
Analyse multiparametrique de particules.
PATENT ASSIGNEE:
SYNTEX (U.S.A.) INC., (200860), 3401 Hillview Avenue, Palo Alto California 94303, (US), (applicant designated states: DE;ES;FR;GB)
INVENTOR:
Vorpahl, John, 427 Ann Court, Livermore, CA 94550, (US)
Ghazarossian, Vartan, 340 Olive Street, Menlo Park, CA 94025, (US)
Ullman, Edwin F., 135 Selby Lane, Atherton, CA 94025, (US)
LEGAL REPRESENTATIVE:
Armitage, Ian Michael et al (27761), MEWBURN ELLIS 2 Cursitor Street, London EC4A 1BQ, (GB)
PATENT (CC, No, Kind, Date): EP 348191 A1 891227 (Basic)
EP 348191 B1 940223
APPLICATION (CC, No, Date): EP 89306290 890622;
PRIORITY (CC, No, Date): US 210688 880623
DESIGNATED STATES (Pub A): AT; BE; CH; DE; ES; FR; GB; IT; LI; NL; SE;
(Pub B): DE; ES; FR; GB
INTERNATIONAL PATENT CLASS: G01N-033/537; G01N-033/551; G01N-033/554; G01N-033/555; G01N-033/80;

ABSTRACT EP 348191 A1
A method for **determining** the presence of a specific binding member bound to first particles in a liquid medium is disclosed. The method comprises providing in combination (1) a liquid medium suspected

of containing a specific binding member bound to first particles, (2) means for agglutinating the first particles in relation to the presence of the specific binding member, and (3) second particles having the same or a different specific binding member for said means for agglutinating bound thereto, thereby providing for said means to agglutinate the second particles. Agglutination of the first and second particles are separately **detectible** and distinguishable by spectroscopic **measurement**. The medium is **incubated** and agglutination of each of the particles is **determined** spectroscopically without separating the first and second particles. The agglutination of the first particles is related to the presence of the specific binding member on the first particles, and the absence of agglutination of the first particles taken together with agglutination of the second particles is related to the absence of the specific binding member on the first particles.

ABSTRACT WORD COUNT: 180

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	554
CLAIMS B	(German)	EPBBF1	571
CLAIMS B	(French)	EPBBF1	647
SPEC B	(English)	EPBBF1	6263
Total word count - document A			0
Total word count - document B			8035
Total word count - documents A + B			8035

8/3,AB/19 (Item 17 from file: 348)
DIALOG(R)File 348:European Patents

00355723
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Barbiturate assay, tracers, immunogens and antibodies.
Test, Indikatoren, Immunogene und Antikorper fur Barbiturate.
Essai, traceurs, immunogenes et anticorps pour barbiturates.
PATENT ASSIGNEE:
ABBOTT LABORATORIES, (225073), One Abbott Park Road, Abbott Park, IL 60064-3500, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;IT;LI;NL)
INVENTOR:
Adamczyk, Maciej Bogdan, 2015 Sprucewood Lane, Lindenhurst Illinois 60046, (US)
Dubler, Robert Edward, 860 Greenleaf, Gurnee Illinois 60031, (US)
Cantarero, Luis Augusto, 1319 Dunleer, Mundelein Illinois 60060, (US)
Jonas, Patrick Francis, 1608 Alexander Court, Waukegan Illinois 60085, (US)
LEGAL REPRESENTATIVE:

Modiano, Guido et al (40782), MODIANO, JOSIF, PISANTY & STAUB Modiano & Associati Via Meravigli, 16, I-20123 Milano, (IT)
PATENT (CC, No, Kind, Date): EP 373508 A2 900620 (Basic)
EP 373508 A3 920708
APPLICATION (CC, No, Date): EP 89122573 891207;
PRIORITY (CC, No, Date): US 284781 881212
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; IT; LI; NL
INTERNATIONAL PATENT CLASS: C07D-493/10; G01N-033/532; G01N-033/542; G01N-033/94; C07D-493/10; C07D-311/00; C07D-307/00

ABSTRACT EP 373508 A2

The present invention is directed to a fluorescence polarization immunoassay for barbiturates, to the various components needed for preparing and carrying out such an assay, and to methods of making these components. Specifically, tracers, immunogens and antibodies are disclosed, as well as methods for preparing them. The tracers and the immunogens are made from substituted barbiturate compounds. A fluorescein moiety is included in the tracer, while a poly(amino acid) forms a part of the immunogen. The assay is conducted by **measuring** the degree of polarization retention of plane-polarized light that has been passed through a sample containing antiserum and tracer. (see image in original document)

ABSTRACT WORD COUNT: 109

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	648
SPEC A	(English)	EPABF1	8640
Total word count - document A			9288
Total word count - document B			0
Total word count - documents A + B			9288

8/3,AB/20 (Item 18 from file: 348)
DIALOG(R)File 348:European Patents

00308092

Assay method using particles with associated fluorescer.
Versuchsmethode unter Verwendung von Partikeln mit assoziiertem, fluoreszierendem Stoff.
Methode d'essai utilisant des particules associees a une substance fluorescente.
PATENT ASSIGNEE:
SYNTEX (U.S.A.) INC., (200862), 3401 Hillview Avenue P.O. Box 10850, Palo Alto California 94303, (US), (applicant designated states: BE;CH;DE;ES;FR;GB;IT;LI;NL;SE)

INVENTOR:
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Kirakossian, Hrair, 4851 Williams Road, San Jose, CA 95129, (US)
Ullman, Edwin F., 135 Selby Lane, Atherton, CA 94025, (US)
LEGAL REPRESENTATIVE:
Armitage, Ian Michael et al (27761), MEWBURN ELLIS & CO. 2/3 Cursitor Street, London EC4A 1BQ, (GB)
PATENT (CC, No, Kind, Date): EP 275139 A2 880720 (Basic)
EP 275139 A3 880803
EP 275139 B1 920415
APPLICATION (CC, No, Date): EP 88300033 880105;
PRIORITY (CC, No, Date): US 925 870107
DESIGNATED STATES: BE; CH; DE; ES; FR; GB; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: G01N-033/58; G01N-033/542; G01N-033/537; G01N-033/543;

ABSTRACT EP 275139 A2
Assay methods are provided or **determining** an analyte in a sample suspected of containing the analyte. The method is carried out using a composition that includes a conjugate of a first sbp member with a particle. A luminescer is reversibly associated with a nonaqueous phase of the particle. Where the first spb member is not complementary to the analyte, a second sbp member that is capable of binding to the first sbp member is employed. Unbound conjugate is separated from conjugate that is bound to the analyte or to the second sbp member. A reagent for enhancing the **detectability** of the luminescer is added and the light emission of the luminescer acted on by the reagent is **measured**.
ABSTRACT WORD COUNT: 122

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	1468
CLAIMS B	(German)	EPBBF1	1471
CLAIMS B	(French)	EPBBF1	1673
SPEC B	(English)	EPBBF1	11713
Total word count - document A			0
Total word count - document B			16325
Total word count - documents A + B			16325

8/3,AB/21 (Item 19 from file: 348)
DIALOG(R)File 348:European Patents

00299248

Method of gene mapping.

Verfahren zur Genkartierung.
Methode de mise en carte de genes.
PATENT ASSIGNEE:
E.I. DU PONT DE NEMOURS AND COMPANY, (200580), 1007 Market Street, Wilmington Delaware 19898, (US), (applicant designated states: BE;DE;FR;GB;GR;IT;LU;NL)
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Brenner, Sydney, 17B, St. Edward's Passage, Cambridge CB2 3PJ, (GB)
LEGAL REPRESENTATIVE:
von Kreisler, Alek, Dipl.-Chem. et al (12434), Patentanwalte von Kreisler-Selting-Werner Postfach 10 22 41, D-50462 Koln, (DE)
PATENT (CC, No, Kind, Date): EP 309969 A2 890405 (Basic)
EP 309969 A3 910306
EP 309969 B1 950719
APPLICATION (CC, No, Date): EP 88115842 880927;
PRIORITY (CC, No, Date): US 103105 870928; US 185741 880425
DESIGNATED STATES: BE; DE; FR; GB; GR; IT; LU; NL
INTERNATIONAL PATENT CLASS: C12Q-001/68;

ABSTRACT EP 309969 A2
The method described characterizes each DNA segment to be mapped by cleaving it to produce DNA fragments which are then end labeled with a reporter(s) specific to the end nucleotides of each fragment. The labeled fragments are again cleaved to produce short fragments which are separated according to size. The short fragments are analyzed as to reporter identity and size which is indicative of the character of each fragment. By derivatizing the cleaved ends of the primary cleaved fragments, the labeling may be delayed until the second cleavage. Prior to labeling the derivatized fragments, all underivatized fragments are removed, the derivatized fragments being immobilized.
ABSTRACT WORD COUNT: 108

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	1565
SPEC A	(English)	EPABF1	24169
Total word count - document A			25734
Total word count - document B			0
Total word count - documents A + B			25734

8/3,AB/22 (Item 20 from file: 348)
DIALOG(R)File 348:European Patents

00293967

ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Non-metal colloidal particle immunoassay.
Immunoassay mit Verwendung von nichtmetallischen, kolloidalen Teilchen.
Essai immunologique utilisant des particules colloidales non-metalliques.
PATENT ASSIGNEE:
ABBOTT LABORATORIES, (225071), , Abbott Park, Illinois 60064, (US),
(applicant designated states: AT;BE;CH;DE;ES;FR;GB;IT;LI;NL)
INVENTOR:
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Yang, Heechung, 1801 Belmont Drive, Green Oaks, IL 60048, (US)
LEGAL REPRESENTATIVE:
Modiano, Guido, Dr.-Ing. et al (40783), Baaderstrasse 3, D-80469 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 298368 A2 890111 (Basic)
EP 298368 A3 910109
EP 298368 B1 941117
APPLICATION (CC, No, Date): EP 88110459 880630;
PRIORITY (CC, No, Date): US 72084 870709
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; IT; LI; NL
INTERNATIONAL PATENT CLASS: G01N-033/58; G01N-033/546; G01N-033/76

ABSTRACT EP 298368 A2
A method of performing a diagnostic immunoassay utilizing colloidal non-metal particles having conjugated thereto a binding component capable of specifically recognizing an analyte to be **determined**. After reaction of the sample and colloidal non-metal particles, the presence or amount of analyte/colloidal non-metal particle complexes are **determined** by optical analysis as a **measure** of the amount of analyte in the sample. The method can be utilized for the specific **detection** of numerous analytes and is sensitive and has a wide **detection** range.
ABSTRACT WORD COUNT: 85

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	309
SPEC A	(English)	EPABF1	2893
Total word count - document A			3202
Total word count - document B			0
Total word count - documents A + B			3202

8/3,AB/23 (Item 21 from file: 348)
DIALOG(R)File 348:European Patents

00287040

Searcher : Shears 308-4994

Fluorescence polarization assay for cyclosporin A and metabolites and related immunogens and antibodies.

Fluoreszenz-Polarisations-Test fur Cyclosporin A und Metaboliten und verwandte Immunogene und Antikorper.

Essais de polarisation par fluorescence pour cyclosporine A et les metabolites et immunogenes et anticorps apparentes.

PATENT ASSIGNEE:
ABBOTT LABORATORIES, (225071), , Abbott Park Illinois 60064, (US), (applicant designated states: BE;CH;DE;ES;FR;GB;IT;LI)

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Morrison, Marjorie Anne, 204 Seafarer Drive, Grayslake Illinois 60030, (US)

LEGAL REPRESENTATIVE:
Modiano, Guido et al (40782), MODIANO, JOSIF, PISANTY & STAUB Modiano & Associati Via Meravigli, 16, I-20123 Milan, (IT)

PATENT (CC, No, Kind, Date): EP 283801 A2 880928 (Basic)
EP 283801 A3 900530
APPLICATION (CC, No, Date): EP 88103397 880304;
PRIORITY (CC, No, Date): US 31494 870327
DESIGNATED STATES: BE; CH; DE; ES; FR; GB; IT; LI
INTERNATIONAL PATENT CLASS: C07K-007/64; G01N-033/68; G01N-033/58;

ABSTRACT EP 283801 A2

The present invention is directed to a fluorescence polarization immunoassay for cyclosporin A and metabolites thereof. The present invention also relates to novel cyclosporin A derivative compounds useful in fluorescence polarization techniques. Included among the novel compounds are cyclosporin A derivatives where the amino acid in the first position is altered. The cyclosporin A derivatives are useful in forming immunogens for raising antibodies specific to cyclosporin A and metabolites thereof.

ABSTRACT WORD COUNT: 74

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	488
SPEC A	(English)	EPABF1	6268
Total word count - document A			6756
Total word count - document B			0
Total word count - documents A + B			6756

00253121
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
HEPATOCYTE DIRECTED VESICLE DELIVERY SYSTEM.
VERABREICHUNGSSYSTEM MIT AUF HEPATOCYTEN GERICHTETEN VESIKELN.
SYSTEME D'ADMINISTRATION DE VESICULES DIRIGEES VERS LES HEPATOCYTES.
PATENT ASSIGNEE:
GEHO, W., Blair, (883090), 533 Beechwood Street, Wooster, OH 44691, (US),
(applicant designated states: DE;FR;GB;IT)
LAU, John R., (883080), 1634 Morgan Street, Wooster, OH 44691, (US),
(applicant designated states: DE;FR;GB;IT)
INVENTOR:
GEHO, W., Blair, 533 Beechwood Street, Wooster, OH 44691, (US)
LAU, John R., 1634 Morgan Street, Wooster, OH 44691, (US)
LEGAL REPRESENTATIVE:
Patentanwalte Beetz sen. - Beetz jun. Timpe - Siegfried -
Schmitt-Fumian- Mayr (100712), Steinsdorfstrasse 10, W-8000 Munchen 22,
(DE)
PATENT (CC, No, Kind, Date): EP 274467 A1 880720 (Basic)
EP 274467 A1 880803
EP 274467 B1 920520
WO 8800474 880128
APPLICATION (CC, No, Date): EP 86904629 860710; WO 86US1421 860710
PRIORITY (CC, No, Date): EP 86904629 860710; WO 86US1421 860710
DESIGNATED STATES: DE; FR; GB; IT
INTERNATIONAL PATENT CLASS: A61K-049/00;
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	612
CLAIMS B	(German)	EPBBF1	551
CLAIMS B	(French)	EPBBF1	705
SPEC B	(English)	EPBBF1	7977
Total word count - document A			0
Total word count - document B			9845
Total word count - documents A + B			9845

8/3,AB/25 (Item 23 from file: 348)
DIALOG(R)File 348:European Patents

00239852
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Detection of haptens in immunoassay techniques.
Nachweis von Haptenen in Immunotestverfahren.
Detection d'haptenes dans des techniques d'immunoessai.
PATENT ASSIGNEE:
Research Corporation, (224863), Suite 853, 25 Broadway, New York New York
Searcher : Shears 308-4994

10174, (US), (applicant designated states:
AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
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DeBusk, A. Gib, 3583 Doris Drive, Tallahasse Florida, (US)
Pegg, R. Kevin, 61 Flint Ridge, Hillsborough North Carolina, (US)
Coleman, R. Marie, 1072 Tallavana Trail, Havana Florida, (US)
Saunders, Mary S., 417 Doggett Drive, Graham North Carolina, (US)
LEGAL REPRESENTATIVE:
Patentanwalte Grunecker, Kinkeldey, Stockmair & Partner (100721),
Maximilianstrasse 58, D-8000 Munchen 22, (DE)
PATENT (CC, No, Kind, Date): EP 242589 A2 871028 (Basic)
EP 242589 A3 890315
APPLICATION (CC, No, Date): EP 87103975 870318;
PRIORITY (CC, No, Date): US 841068 860318
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/00; C12N-005/00; C12P-021/00;
C07K-015/00; G01N-033/577; G01N-033/543; C12P-021/00; C12R-001/91

ABSTRACT EP 242589 A2
The present invention relates to a method of producing monoclonal antibodies capable of being utilized in hapten sandwich assays, and the antibodies produced by this method. It also relates to a method of **detecting** haptens by utilizing these antibodies in a sandwich assay. Also provided is a method of hapten **detection** in a nonaqueous sample.
ABSTRACT WORD COUNT: 59

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	899
SPEC A	(English)	EPABF1	12052
Total word count - document A			12951
Total word count - document B			0
Total word count - documents A + B			12951

8/3,AB/26 (Item 24 from file: 348)
DIALOG(R)File 348:European Patents

00224921
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Particle separation method.
Teilchentrennungsverfahren.
Procede de separation de particules.
PATENT ASSIGNEE:

SYNTEX (U.S.A.) INC., (200860), 3401 Hillview Avenue, Palo Alto California 94303, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:
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Ghazarossian, Vartan E., 2642 Ramona Street, Palo Alto California, (US)
Weng, Litai, 1416 San Luis Avenue, Mountain View California, (US)
LEGAL REPRESENTATIVE:
Armitage, Ian Michael et al (27761), MEWBURN ELLIS & CO. 2/3 Cursitor Street, London EC4A 1BQ, (GB)
PATENT (CC, No, Kind, Date): EP 230768 A1 870805 (Basic)
EP 230768 B1 920318
APPLICATION (CC, No, Date): EP 86309967 861219;
PRIORITY (CC, No, Date): US 811202 851220
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: B03C-001/00; G01N-033/553; G01N-033/538; G01N-033/78; G01N-033/569

ABSTRACT EP 230768 A1

A method is disclosed for separating a substance from a liquid medium. The method comprises combining the liquid medium containing the substance with magnetic particles under conditions for non-specific chemical binding of the magnetic particles. Thereafter, the medium is subjected to a magnetic field gradient to separate the particles from the medium. The preferred non-specific binding is achieved as the result of charge interactions between the particles usually by means of a polyionic reagent. The method of the invention has particular application to the separation of cells and microorganisms from aqueous suspensions and also to the **determination** of an analyte in a sample suspected of containing the analyte. The analyte is a member of a specific binding pair (sbp). The sample is combined in an assay medium with magnetic particles and a sbp member complementary to the analyte. Magnetic or non-magnetic particles capable of specific binding to the analyte or its complementary sbp member must be included in the assay medium. The combination is made under conditions for non-specifically aggregating the magnetic particles or coaggregating the magnetic and non-magnetic particles when non-magnetic particles are present. The assay medium is subjected to a magnetic field gradient to separate the aggregated particles from the medium. Then, the medium or the particles are examined for the presence or amount of the analyte or an sbp member, the binding of which is affected by the presence of the analyte.
ABSTRACT WORD COUNT: 239

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:
Available Text Language Update Word Count
CLAIMS B (English) EPBBF1 715
CLAIMS B (German) EPBBF1 720

CLAIMS B	(French)	EPBBF1	796
SPEC B	(English)	EPBBF1	12651
Total word count - document A			0
Total word count - document B			14882
Total word count - documents A + B			14882

8/3,AB/27 (Item 25 from file: 348)
DIALOG(R)File 348:European Patents

00222019
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Homogeneous assay for specific polynucleotides and kit for performing same.
Homogenes Testsystem fur spezifische Polynukleotide und Kit dafur.
Essai homogene pour des polynucleotides specifiques et trousse pour son application.
PATENT ASSIGNEE:
SYNTEX (U.S.A.) INC., (200860), 3401 Hillview Avenue, Palo Alto California 94303, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:
Kurn, Nurith, 978 Blair Court, Palo Alto California 94303, (US)
Bahl, Chander, 5 Jenny Jump Court, Flemington New Jersey 08822, (US)
Ullman, Edwin F., 135 Selby Lane, Atherton California, (US)
LEGAL REPRESENTATIVE:
Armitage, Ian Michael et al (27761), MEWBURN ELLIS York House 23 Kingsway , London WC2B 6HP, (GB)
PATENT (CC, No, Kind, Date): EP 224995 A1 870610 (Basic)
EP 224995 B1 920212
APPLICATION (CC, No, Date): EP 86306860 860905;
PRIORITY (CC, No, Date): US 773386 850906
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12Q-001/68

ABSTRACT EP 224995 A1
A method for **determining** the presence of a polynucleotide analyte in a sample suspected of containing the analyte is disclosed. The method comprises combining in an assay medium the sample and first and second polynucleotide reagents complementary to the analyte. Each of the first and second reagents hybridize with a different region of the analyte. The first reagent contains means for rendering the first reagent non-covalently polymerizable. The second reagent contains means for rendering the second reagent **detectable**. The sample and the first and second reagents are combined in the assay medium under conditions for polymerizing the first reagent wherein the second reagent becomes bound to the polymerized first reagent only when the analyte is present in the sample. A **determination** is then made as to whether the second reagent has become bound to the polymerized first reagent. The method has

broad application for **determining** the presence of a polynucleotide analyte such as DNA, RNA, the genomes of viruses, bacteria, molds, fungi, and fragments thereof, and the like. Preferred means for rendering the first reagent non-covalently polymerizable includes a repeating oligonucleotide sequence covalently bound to the first reagent.
ABSTRACT WORD COUNT: 192

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPAB95	767
CLAIMS B	(German)	EPAB95	753
CLAIMS B	(French)	EPAB95	888
SPEC B	(English)	EPAB95	7866
Total word count - document A			0
Total word count - document B			10274
Total word count - documents A + B			10274

8/3,AB/28 (Item 26 from file: 348)
DIALOG(R)File 348:European Patents

00217225
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Fluorescent labels and labeled species and their use in analytical elements and **determinations**.
Fluoreszierende Indikatoren und Kennsatz-Spezies und ihre Verwendung in analytischen Elementen und Bestimmungen.
Indicateurs fluorescents et les especes marques et leur utilisation dans les elements analytiques et les **determinations**.
PATENT ASSIGNEE:
EASTMAN KODAK COMPANY (a New Jersey corporation), (201210), 343 State Street, Rochester New York 14650, (US), (applicant designated states: CH;DE;FR;GB;LI)
INVENTOR:
Burdick, Brent Arthur, Kodak Park, Rochester, NY, (US)
Danielson, Susan Jean, Kodak Park, Rochester, NY, (US)
LEGAL REPRESENTATIVE:
Nunney, Ronald Frederick Adolphe et al (34411), Kodak Limited Patent Department Headstone Drive, Harrow Middlesex HA1 4TY, (GB)
PATENT (CC, No, Kind, Date): EP 195624 A2 860924 (Basic)
EP 195624 A3 890809
EP 195624 B1 920819
APPLICATION (CC, No, Date): EP 86301904 860317;
PRIORITY (CC, No, Date): US 713206 850318
DESIGNATED STATES: CH; DE; FR; GB; LI
INTERNATIONAL PATENT CLASS: G01N-033/533; G01N-033/58; G01N-033/52;

ABSTRACT EP 195624 A2

Fluorescent labels and labeled species and their use in analytical elements and **determinations**.

Fluorescent labels comprise a polysaccharide bound to a polymeric particle which contains a fluorescent rare earth chelate. These labels can be attached to any of a variety of physiologically reactive species to provide labeled species which have improved stability in aqueous solutions. The labeled species are particularly useful in specific binding assays to **determine** an immunologically reactive **ligand**, e.g. a hapten, in either solution or dry analytical techniques.

ABSTRACT WORD COUNT: 83

LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	512
CLAIMS B	(German)	EPBBF1	498
CLAIMS B	(French)	EPBBF1	548
SPEC B	(English)	EPBBF1	6814
Total word count - document A			0
Total word count - document B			8372
Total word count - documents A + B			8372

8/3,AB/29 (Item 27 from file: 348)

DIALOG(R)File 348:European Patents

00215686

ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348

Method for **measuring** free ligands in biological fluids.

Verfahren zum Messen von Freiliganden in biologischen Flussigkeiten.

Procede pour **determiner** les ligands libres dans les fluides biologiques.

PATENT ASSIGNEE:

DIAGNOSTIC PRODUCTS CORPORATION, (728210), 5700 West 96th Street, Los Angeles California 90045, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;LU;NL;SE)

INVENTOR:

Said El Shami, A., 29974 Rolling Ridge Drive, Agoura Hills, CA 91301, (US)

LEGAL REPRESENTATIVE:

Cresswell, Thomas Anthony et al (50352), J.A. KEMP & CO. 14 South Square Gray's Inn, London WC1R 5LX, (GB)

PATENT (CC, No, Kind, Date): EP 218309 A2 870415 (Basic)
EP 218309 A3 880831
EP 218309 B1 951115

APPLICATION (CC, No, Date): EP 86300336 860117;

Searcher : Shears 308-4994

PRIORITY (CC, No, Date): US 784857 851004
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: G01N-033/53; G01N-033/74

ABSTRACT EP 218309 A2

A method for **measuring** the concentration of a free **ligand** in a biological fluid in the presence of bound **ligand** and endogenous binding proteins, without disturbing the equilibrium between free **ligand** and protein-bound **ligand**, which comprises (a) **incubating** a sample of biological fluid with (i) a **ligand** analog tracer which due to its chemical structure, does not bind to some of the endogenous binding proteins but does bind to at least one other endogenous binder protein, (ii) a specific **ligand** binder and (iii) at least one specific chemical inhibitor reagent that singly or in combination inhibit the binding of the **ligand** analog tracer to said at least one other endogenous binding protein; (b) separating the **ligand** analog tracer bound to the specific binder from unbound tracer; and (c) **determining** the concentration of free **ligand** in said biological fluid.

ABSTRACT WORD COUNT: 142

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	564
CLAIMS B	(English)	EPAB95	347
CLAIMS B	(German)	EPAB95	315
CLAIMS B	(French)	EPAB95	381
SPEC A	(English)	EPABF1	5126
SPEC B	(English)	EPAB95	4006
Total word count - document A			5690
Total word count - document B			5049
Total word count - documents A + B			10739

8/3,AB/30 (Item 28 from file: 348)
DIALOG(R)File 348:European Patents

00199419
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Ethosuximide assay tracers, immunogens and antibodies.
Probe, Tracers, Immunogene und Antikorper von Ethosuximid.
Dosage, traceurs, immunogenes et anticorps de l'ethosuximide.
PATENT ASSIGNEE:
ABBOTT LABORATORIES, (225070), 14th Street and Sheridan Road North St, North Chicago, Illinois 60064, (US), (applicant designated states: BE;DE;FR;IT)
INVENTOR:

Heiman, Daniel Feulner, 407 Drake, Libertyville Illinois 60048, (US)
Cantarero, Luis A., 1319 Dunleer, Mundelein Illinois 60060, (US)
Chan, Clifford Man, 17652 West Windslow Drive, Grayslake Illinois 60030, (US)
LEGAL REPRESENTATIVE:
Modiano, Guido et al (40782), MODIANO, JOSIF, PISANTY & STAUB Modiano & Associati Via Meravigli, 16, I-20123 Milano, (IT)
PATENT (CC, No, Kind, Date): EP 199963 A1 861105 (Basic)
EP 199963 B1 911023
APPLICATION (CC, No, Date): EP 86103673 860318;
PRIORITY (CC, No, Date): US 718601 850401
DESIGNATED STATES: BE; DE; FR; IT
INTERNATIONAL PATENT CLASS: G01N-033/58; G01N-033/533; C07D-493/10; C07K-015/00;

ABSTRACT EP 199963 A1

The present invention is directed to a fluorescence polarization assay for ethosuximide, to the various components needed for preparing and carrying out such an assay, and to methods of making these components. Specifically, tracers, immunogens and antibodies are disclosed, as well as methods for making them. The tracers and the immunogens are made from analogs and derivatives of ethosuximide. A fluorescein moiety is included in the tracer while a poly(amino acid) forms a part of the immunogen. The assay is conducted by **measuring** the degree of polarization of plane polarized light that has been passed through a sample containing antiserum and tracer.

ABSTRACT WORD COUNT: 106

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	621
CLAIMS B	(German)	EPBBF1	547
CLAIMS B	(French)	EPBBF1	737
SPEC B	(English)	EPBBF1	10081
Total word count - document A			0
Total word count - document B			11986
Total word count - documents A + B			11986

8/3,AB/31 (Item 29 from file: 348)
DIALOG(R)File 348:European Patents

00195383
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
METHODS FOR PROTEIN BINDING ENZYME COMPLEMENTATION ASSAYS.
ERGANZUNGSTESTVERFAHREN VON PROTEINE BINDENDEN ENZYMEN.
PROCEDES D'ANALYSES DE COMPLEMENTATION D'ENZYMES DE LIAISON DE PROTEINES.

PATENT ASSIGNEE:
MICROGENICS CORPORATION (a Delaware corporation), (1168360), 2380A Bisso Lane, Concord California 94520, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:
HENDERSON, Daniel Robert, 216 Chadwick Way, Benicia, CA 95410, (US)
LEGAL REPRESENTATIVE:
Ahner, Francis et al (13601), CABINET REGIMBEAU, 26, avenue Kleber, F-75116 Paris, (FR)
PATENT (CC, No, Kind, Date): EP 199801 A1 861105 (Basic)
EP 199801 A1 890201
EP 199801 B1 930825
WO 8602666 860509
APPLICATION (CC, No, Date): EP 85905685 851028; WO 85US2095 851028
PRIORITY (CC, No, Date): US 666080 841029; US 721267 850408; US 788370 851022
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12Q-001/70; G01N-033/53; C12Q-001/54; C12Q-001/34; C12Q-001/26; C12P-021/00; C12P-021/02; C12N-015/00; C12N-001/20; C12N-001/00; C12R-001/19;
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	1928
CLAIMS B	(German)	EPBBF1	1858
CLAIMS B	(French)	EPBBF1	2203
SPEC B	(English)	EPBBF1	20154
Total word count - document A			0
Total word count - document B			26143
Total word count - documents A + B			26143

8/3,AB/32 (Item 30 from file: 348)
DIALOG(R)File 348:European Patents

00155403
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
DETECTING AGENT CARRYING POLYMER HAVING MULTIPLE UNITS OF VISUALIZATION MONOMER.
MIT EINEM NACHWEISAGENS VERSEHENES POLYMER, DAS AUS MEHREREN VISUALISIERUNGSMONOMEREN BESTEHT.
POLYMERE PORTEUR D'UN AGENT DE **DETECTION** ET POSSEDANT DES UNITES MULTIPLES D'UN MONOMERE DE VISUALISATION.
PATENT ASSIGNEE:
YALE UNIVERSITY, (479553), 260 Whitney Avenue P.O. Box 6666, New Haven Connecticut 06511, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;LI;LU;NL;SE)
INVENTOR:

WARD, David, C., 40 Peddler's Road, Guilford, CT 06437, (US)
LEARY, Joseph, J., 4B Birch Lane, East Haven, CT 06512, (US)
BRIGATI, David, J., 1213 Julianne Drive, Hummelstown, PA 17036, (US)
LEGAL REPRESENTATIVE:
Vossius & Partner (100311), Siebertstrasse 4 P.O. Box 86 07 67, W-8000 Munchen 86, (DE)
PATENT (CC, No, Kind, Date): EP 149654 A1 850731 (Basic)
EP 149654 A1 880629
EP 149654 B1 920909
WO 8404970 841220
APPLICATION (CC, No, Date): EP 84902738 840608; WO 84US888 840608
PRIORITY (CC, No, Date): US 503298 830610
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: G01N-033/50; G01N-033/52; G01N-033/536; G01N-033/58;
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	4004
CLAIMS B	(German)	EPBBF1	3718
CLAIMS B	(French)	EPBBF1	4891
SPEC B	(English)	EPBBF1	15026
Total word count - document A			0
Total word count - document B			27639
Total word count - documents A + B			27639

8/3,AB/33 (Item 31 from file: 348)
DIALOG(R)File 348:European Patents

00148438
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Magnetic particles for use in separations.
Magnetische Teilchen zur Verwendung in Trennungen.
Particules magnetiques pour l'utilisation dans des separations.
PATENT ASSIGNEE:
ADVANCED MAGNETICS INCORPORATED (a Delaware corp.), (610332), 61 Mooney Street, Cambridge Massachussets, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;NL;SE)
INVENTOR:
Chagnon, Mark Steven, c/o Advanced Magnetics, Inc. 45 Spinelli Place, Cambridge Massachusetts 02138, (US)
Groman, Ernest Victor, 80 Columbia Street, Brookline Massachusetts, (US)
Josephson, Lee, 11 Martin Street, Arlington Massachusetts, (US)
Whitehead, Roy Arthur, 626 Main Street, Hingham Massachusetts, (US)
LEGAL REPRESENTATIVE:
Warcoin, Jacques (19071), Cabinet Regimbeau 26, avenue Kleber, F-75116 Paris, (FR)

PATENT (CC, No, Kind, Date): EP 125995 A2 841121 (Basic)
EP 125995 A3 861230
EP 125995 B1 911211
APPLICATION (CC, No, Date): EP 84400952 840510;
PRIORITY (CC, No, Date): US 493991 830512
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: G01N-033/553; B01D-015/08; H01F-001/00; C12Q-001/00;

ABSTRACT EP 125995 A2
Magnetic particles for use in separations.
A process is provided for the preparation of magnetic particles to which a wide variety of molecules may be coupled. The magnetic particles can be dispersed in aqueous media without rapid settling and conveniently reclaimed from media with a magnetic field. Preferred particles do not become magnetic after application of a magnetic field and can be redispersed and reused. The magnetic particles are useful in biological systems involving separations.
ABSTRACT WORD COUNT: 77

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	1246
CLAIMS B	(German)	EPBBF1	1416
CLAIMS B	(French)	EPBBF1	1475
SPEC B	(English)	EPBBF1	11279
Total word count - document A			0
Total word count - document B			15416
Total word count - documents A + B			15416

8/3,AB/34 (Item 1 from file: 156)
DIALOG(R)File 156:Toxline(R)

01907337 Subfile: TOXBIB-95-028753
Thyroid hormones and regulation of cell reliability systems.
Antipenko AYe; Antipenko YN
Institute of Physiology, St. Petersburg University, Russia.
Source: Adv Enzyme Regul; VOL 34, 1994, P173-98 ISSN: 0065-2571 Coden: 2LG
Language: ENGLISH
Document Type: JOURNAL ARTICLE
Data and arguments are presented that provide evidence of a role played by thyroid hormones (TH) in cell reliability improvement. This role may be determined by synergistic TH action on the following key cell reliability systems: (1) reactive oxygen species (ROS) attack inhibition, and (2) genetic structure repair from injuries inflicted in the course of

endogenous and induced mutagenesis. (1) New approaches to ROS oxidation defence were examined. It has been shown that Ca(2+)-ATPase and, probably, regulatory proteins of cell membranes may be the main target for oxidative attack. Protein phosphorylation as well as use of dithiothreitol will lead to a protective action against Ca2+ transport damaging in aorta smooth muscle sarcoplasmic reticulum under oxidation by HOCl, the most toxic ROS of activated neutrophils, whereas **thyroxine** (T4) and 3,5,3'-**triiodothyronine** (T3) validly inhibit chemiluminescence in human neutrophils activated by pyrogenal, a lipopolysaccharide from Salmonella typhi cell wall. As this takes place, TH most likely block neutrophil stimulation at the receptor-**ligand** interaction level. In this case L-T4 and L-T3 antioxidative effect is greater than that of DL-**thyroxine** and much greater than that produced by such a potent antioxidant as 4-methyl-2,6-diisobutyl phenol. (2) T4 acts as reparogen in rat liver cells under X-ray irradiation when a dose measuring one-half of daily hormone production by the normally functioning thyroid gland is administered to animals. Ionizing radiation dose reduction factor reached 1.3-1.4 following T4 administration. Reparogenic effect of T4 persists for at least 2 months from the moment the hormone has been administered and can be reduced in the presence of **dinitrophenol**. It is important to note that antioxidant and reparogenic TH potential can manifest itself within the range of physiologic concentrations of these hormones. Therefore, stimulation of cell reliability systems with TH may prove to be important for correcting conditions caused by errors in energy- and Ca(2+)-dependent DNA repair under extensive ROS attack. In particular, taking into account different responsiveness of normal and neoplastic tissues to TH, the use of TH reparogenic as well as antioxidant potential may contribute significantly to the improvement of antitumor radiotherapy efficacy.

8/3,AB/35 (Item 2 from file: 156)
DIALOG(R)File 156:Toxline(R)

01875951 Subfile: TOXBIB-94-049158
A naturally occurring furan fatty acid enhances drug inhibition of **thyroxine** binding in serum.
Lim CF; Stockigt JR; Curtis AJ; Wynne KN; Barlow JW; Topliss DJ
Ewen Downie Metabolic Unit, Alfred Hospital, Melbourne, Victoria, Australia.
Source: Metabolism; VOL 42, ISS 11, 1993, P1468-74 ISSN: 0026-0495 Coden: MUM
Language: ENGLISH
Document Type: JOURNAL ARTICLE
We studied the **thyroxine** (T4)-displacing effects of a naturally occurring, highly albumin-bound furanoid acid that accumulates in serum in renal failure to concentrations in excess of 0.2 mmol/L. This substance, 3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid (CMPF), has been shown to displace acidic drugs from albumin binding. The effects of CMPF on